Appendix 1

Mr Richardson's Report

COT MATTRESS BIODETERIORATION AND TOXIC GAS GENERATION
a possible cause of
Sudden lnfant Death Syndrome

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A report submitted to the Group of Experts
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Chairman: Lady Limerick
(Summary and Recommendations pages 36-38)

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COT MATTRESS BIODETERIORATION AND TOXIC GAS GENERATION

a possible cause of Sudden lnfant Death Syndrome

CONTENTS

VORWORT

Barry A Richardson, der Autor dieses Berichtes, ist ein wissenschaftlicher Gutachter, der sich auf die Erforschung und gerichtsmedizinische Untersuchungen von Defekten und Verrottung von Materialien, Behandlungssysteme wie Pestizide und Flammschutzmittel und damit zusammenhängende Gesundheitsprobleme spezialisiert hat. Gegenwärtig arbeitet er in einer Privatpraxis in Winchester, England, und als Technischer Direktor der *Penarth Research International Limited* in Guernsey (Kanalinseln).

Barry Richardson machte seine Abschlußprüfung 1960 an der *University of Southampton* als *Bachelor of Science* in Physik, Zoologie, Physiologie und Biochemie. Seine *postgraduate research* in der Industrie über die Verrottung von Holz wurde durch seine Berufung als *Associate* des *Institute o Wood Science* anerkannt und seine späteren Untersuchungen durch seine Beförderung zum *Fellow* des Instituts. Als wissenschaftlicher Gutachter arbeitet er seit 1965 und war von 1983-85 Vorsitzender des *Council of the Association of Consulting Scientists,* ist gegenwärtig *Honorary Secretary* der *Association* und einer ihrer Repräsentanten beim *Parliamentary & Scientific Committee at Westminster.* Seine Forschung war nicht auf Holz und Holzbehandlung, wie Konservierungs- und Flammschutzmittel, beschränkt, sondern betraf vielerlei Materialien. Er ist für seine Arbeiten über Mauerwerk gut bekannt und war seit 1966 Gutachter für die *Commonwealth War Graves Commission.* Zu seiner Forschung gehörten Untersuchungen der Aktionsmechanismen verschiedener Gruppen von Chemikalien in Bezug auf ihre Konservierungseigenschaften, ihre Toxizität gegenüber verschiedener Organismen und ihre Gesundheitsgefährdung, einschließlich der Verbindungen von Kupfer, Zink, Chrom, Arsen und Bor, sowie verschiedener Phenole und organischer Verbindungen von Zinn, Blei, Aluminium, Phosphor, Arsen, Antimon und Quecksilber. Er ist der Autor von mehreren hundert Arbeiten, die auf Konferenzen präsentiert oder in wissenschaftlichen Zeitungen publiziert wurden und auch der Verfasser technischer Bücher, einschließlich von *Wood Preservation* (1978, 2. Aufl. 1993), *Remedial Treatment of Buildings* (1980, 2. Aufl. 1995) und *Defects and Deterioration in Buildings* (1991, 2. Aufl. 1998, 3. Aufl. 2003).

1988 verwickelte sich Barry Richardson zufällig in die Erforschung des plötzlichen Kindstodes als er die Verrottung von schwer bestücktem PVC-Material in Marquisen untersuchte. Die Verrottung wurde durch zwei Fungus-Arten verursacht, trotz Anwesenheit des arsenischen Konservierungsmittels OBPA. Er warnte davor, dass die Fungus-Infektion diese Arsenverbindung in extrem giftiges Arsin-Gas umwandeln könnte und verfasste eine Warnung für seine Kunden. Peter Mitchell, ein Hersteller von Marquisen, kontaktierte die Hersteller des Konservierungsmittels, die ihm versicherten, dass OBPA vollkommen ungiftig und sogar zur Verwendung in PVC-Kindermatratzenhüllen zugelassen sei. Peter Mitchell fragte, ob die Verwendung von OBPA Fälle von plötzlichem Kindstod erklären könnte, und Richardson antwortete, das sei möglich, und dass ein besonders häufiger und normalerweise harmloser Haushalts-Fungus, *Scopulariopsis brevicaulis,* dafür verantwortlich sein könnte. Man fand, dass alle Kindermatratzen nach einigen Monaten in Gebrauch von diesem Fungus infiziert waren, aber gewöhnlich keine signifikante Generation von Arsine entdeckt werden konnte. OBPA wurde auf den Britischen Inseln in Kindermatratzen normalerweise nicht verwendet. Die PVC-Bedeckung enthielt allerdings Flammschutzmittel auf der Basis von Phosphor- und Antimonverbindungen, und man fand, dass der gleiche Fungus diese Verbindungen in extrem toxische Phosphin- und Stibin-Gase umwandeln konnte; Flammschutzmittel, oft Phosphorverbindungen, wurden auch in gewebten Stoffen, Netz- und Schaumstoff-Materialien gefunden, die in Kindermatratzen verwendet wurden.

Diese Befunde wurden im Frühjahr 1989 vertraulich dem *Department of Health* (dem Britischen Gesundheitsministerium) und der *Foundation for the Study of Infant Deaths* (FSID) mitgeteilt. Der verstorbene Sir Ronald Gibson, ein früherer *Chairman of the Coucil* der *British Medical Association* gab den Rat, eine Warnung an praktizierende Ärzte und Forscher, die sich mit dem plötzlichen Kindstod befaßten, publiziert werden sollte und eine Nachricht wurde an das *British Medical Journal* gegeben. Mittlerweile hatten aber Reporter entdeckt, dass Matratzen zu Untersuchungen versandt wurden, und so wurden Berichte über die Generation giftiger Gase aus Matratzen als mögliche Ursache des plötzlichen Kindstodes im Juni 1989 zuerst von den Medien publiziert, ohne dass der Ärzteschaft irgendeine Erklärung dafür zugänglich war.

Die erste kurze Darstellung der Hypothese wurde im März 1990 im *Lancet* publiziert, und die Anfanguntersuchungen im Juli 1990 der gemeinsamen Konferenz der *British Society for Allergy and Environmental Medicine* (BSAEM) und der *American Academy of Environmental Medicine* (AAEM) vorgetragen, anschließend wurde diese Arbeit in der Zeitschrift (der AAEM) *Environmental Medicine* publiziert. Bei der BSAEM können sich nur praktizierende Ärzte um eine Migliedschaft bewerben, aber Wissenschaftler können ernannt werden, wenn das von der der gesamten Mitgliedschaft bestätigt wird. Barry Richardson wurde in Anerkennung seiner Untersuchungen über den plötzlichen Kindstod auf diese Art zum Mitglied gewählt. Er wurde außerdem zum *Honorary Research Fellow* am *King Alfred College in Winchester* ernannt, was ihm Zugang zur Bibliothek und den Laboratorien gab, aber keine finanzielle Unterstützung; die Untersuchungen zum plötzlichen Kindstod blieben unbezahlt, außer das dreimonatige Teilzeit-Studium der Literatur zu plötzlichen Kindstod 1990, die zum Teil von *Tomy UK Limited* finanziert wurde.

1. INTRODUCTION

1.1 A Cot death is one of the most dreadful events that a family may encounter. The death of an infant is a tragedy but cot death is also sudden, unexpected and unexplained. Parents wonder whether their lack of care may have caused the death, and there is always suspicion, that accidental or deliberate smothering may have been involved; there have been reports by medical researchers as recently as 1989 suggesting that smothering is the cause of most cot deaths! Parents lose confidence in themselves and in each other and become depressed, prompting marital problems. Other children in the family become seriously affected; there are almost always older children in the family as cot deaths are rare amongst first children.

1.2 A steady increase in unexplained infant deaths was first noticed in about 1952, prompting Barrett to propose in 1954 that *'unexpected deaths in sleeping quarters of apparently healthy infants'* should be described as cot death, although the term crib death is preferred in north America. The cot death rates increased steadily, despite intensifying research, and in 1969 Beckwith proposed that 'the sudden death of any infant or young child which is unexpected by history, and in which a thorough post-mortem examination fails to demonstrate an adequate cause of death' should be described as sudden infant death syndrome (SIDS). This description was adopted as code 798.0 in the International Classification of Diseases, and this new item soon appeared in the mortality statistics of affected countries, demonstrating immediately that SIDS is a serious problem in some countries but unknown in others. Cot death rates continued to increase steadily, and it was considered for some years that this was due to increasing recognition and that there was a corresponding reduction in other causes of death. This suggestion was apparently confirmed by the observation that the total mortality rate for SIDS and respiratory diseases in England and Wales remained almost constant for many years but it is now recognised that this was a coincidence and that the reduction in deaths from respiratory diseases actually resulted from the introduction of improved antibiotics, and this same reduction is seen in other age groups and in countries such as Japan where SIDS was uncommon until recently and did not even appear in the statistics.

1.3 The cause of SIDS could not be identified despite intensive investigative research, although epidemiological studies were more successful recently, particularly in identifying contributory factors. The failure to identify a single cause prompted the suggestion that SIDS might be due to many different causes, but the evidence of consistency in the features of SIDS actually suggests a single cause with many contributory factors. The SIDS rate in west Europe, north America and most other western-style countries was about 2 to 4 per 1,000 live births in 1980-90, but SIDS was not recognised at all in many countries including Japan, Russia, China, Thailand, India and parts of Africa. Rates were lower in Hong Kong, a country with mixed values, and amongst infants of African and Asian origin in England and Wales. The rates in Australia and New Zealand were relatively low amongst caucasians but very high amongst aborigines, suggesting an ethnic relationship such as a dietary factor, although recent research indicates a geographical relationship. In Southland in Neew Zealand very high rates were associated with coucasian communities

1.4 It is often suggested that cot deaths are not new and that they have simply attracted more attention in recent years. lt is true that unexplained and unexpected infant deaths are mentioned even in the Bible, and the rates recorded in London were very high at times during the 18 and 19 centuries, but the current cot death problem concerns the high rates of sudden and unexpected infant deaths that have developed in some western-style countries since about 1950 compared with earlier rates and the very low rates in some other

countries. In England and Wales, for example, there were 1,542 SIDS deaths annually in 1986-88, representing a rate of 2.3 deaths per 1,000 live births, but annual unexpected and unexplained deaths must be reduced to below 70, a rate of 0.1, to return to the situation before 1950 or to approach the insignificant numbers of unexplained deaths that were reported in Japan until recently. These figures clearly illustrate the magnitude of the cot death tragedy; Various precautions have been suggested since 1985 and some of these have achieved significant reductions in cot death rates. For example, it was recommended in the Netherlands in 1987 that the prone or face down sleeping position should be avoided, and this prompted a reduction of about 40%, sufficient to indicate that the prone position is a contributory cause of cot death but that the primary cause. The similar Department of Health *Back to Sleep* campaign which was introduced in November 1991 has achieveded similar success, although SIDS deaths had been decreasing for more than two years before.

1.5 There were many sudden unexpected infant deaths in the 19 century. Gosio, an Italian chemist investigating the rooms where the infants had died, noticed a garlic odour which he associated with the Marsh and Gutzeit analytical tests for arsenic. He also noticed that adults were ill with symptoms that he associated with arsenical poisoning, and he detected arsenic when he analysed finger nails and hair in which this element accumulates in chronic poisoning. He identified the source as wallpapers and carpets containing arsenical green pigments which were affected by dampness and a fungus *Penicillium brevicaule*, now known es *Scopulariopsis brevicaulis*. This gaseous arsenic was eventually identified as arsine and related alkyl compounds, and the risk of poisoning in this way was widely recognised; a Royal Commission on arsenic poisoning reported in 1904 that this gaseous poisoning was particularly sinister, difficult to diagnose, and probably undetected in most cases. Precautions were introduced, particularly the prohibition of arsenical pigments, and the last case of death from this cause was reported in the United Kingdom in 1932. Since then the risk of gaseous arsenical poisoning has been forgotten, except by the wood preservation industry in which the risk is potentially very high as arsenic compounds are used in situations in which fungal infections occur.

1.6 There has been a steady increase in cot death since about 1950. Various causes have been suggested but whilst it is now clear that some of these are contributory causes and appropriate precautions can reduce the cot death rate, the primary cause remained unidentified until 1989 when it was suggested that toxic gas generation from mattress materials might be involved. This hypothesis was prompted by Gosio's investigations in the 19 century into sudden unexpected infant deaths and the recognition that similar risks may be associated with deterioration of cot mattress materials containing phosphorus, arsenic and antimony compounds as fire retardents and preservatives, and the biogeneration of phosphines, arsines and stibines by the same common and otherwise harmless fungus that Gosio had identified; the fungus usually converts nitrogen compounds such as proteins into ammonia, and nitrogen, phosphorus, arsenic and antimony are sequential elements in group V/Vb of the chemical periodic table with similar chemical properties.

1.7 It is often suggested that this hypothesis contradicts the findings of extensive cot death research over many years but this is untrue; it is consistend with all reported features of SIDS and identifies a primary cuase which explains other research findings. Whilst it is certain that there will be cot deaths which are not associated with this primary cause, it is likely to be the explanation in most cases that are diagnoses as SIDS. It is also certain that most infants have bee exposed to this hazard but most infants have not died, indicating that this primare cause alone is not sufficient but that other contributory factors must be

involved, particularly the prone sleeping position and hyperthermia caused by overwrapping or Illness.

2 . MATTRESS BIODETERIORATION AND SIDS

2.1 It was recognised by Richardson in 1988 that microbial deterioration of plasticised polyvinyl chloride (PVC) containing an arsenical preservative might result in the generation of extremely toxic gaseous arsines. It was considered that this process might be a cause of sudden infant death. Investigations confirmed that used cot mattresses are naturally infected by fungi which can cause this gas generation and, whilst arsenical preservatives are not normally used in PVC cot mattress coverings in the British Isles, toxic gaseous phosphines and stibines can be similarly generated from the organo-phosphate plasticisers and antimony trioxide that are used when fire resistance is required. Phosphines can also be generated by biodeterioration of woven fabrics, net and foam containing phophate fire retardents. Poisoning by toxic gases generated in this way is consistent with all the known features of SIDS.

The Richardson hypothesis

2.2 The Richardson hypothesis suggests that the primary cause of sudden infant death syndrome (SIDS) is poisoning by gaseous phosphines, arsines and stibines generated by deterioration of cot mattress materials by micro-organisms, particularly *Scopulariopsis brevicaulis*, an otherwise harmless fungus which is normally found in all domestic environments. All cot mattresses become naturally infected in use by micro-organisms, and these toxic gases are generated from all mattress materials that contain phosphorus, arsenic or antimony compounds. Whether an infant is unaffected or suffers irritability, illness or death depends on various contributory factors (Richardson 1990,1991a,b, 1994).

Mattress biodeterioration and toxic gas generation

2.3 In the late 19 century an Italian chemist Gosio discovered that mysterious infant deaths and adult illnesses were caused by a gaseous form of arsenic which was generated by fungal deterioration of arsenical pigments in wallpapers, and white arsenic (arsenious oxide) used as a rodent repellent in horse hoof size used for fixing wallpaper (Gosio 1892,1893,1897; Sanger 1894a,b; Schmidt 1899; Biginelli 1900; Anon. 1932; Thom and Raper 1932). Poisoning by volatile arsenic compounds in this way was recognised about 90 years ago by a Royal Commission on arsenical poisoning as a particularly sinister poisoning and incorrectly diagnosed as toxic jaundice or haemolytic anaemia (Anon. 1904; Hunter 1936; Doig 1958). The fungus involved was *Scopulariopsis brevicaulis*, known at that time as *Penicillium brevicaule*. This fungus, which is commonly found in the domestic environment, generates ammonia from nitrogen compounds such as proteins in meat, cheese and butter, as well as in damp leather and wool (Morton & Smith 1963; Onions 1966). Ammonia is nitrogen trihydride, derived from the nitrogen in the protein substrate, whilst Gosio's arsenic gas was identified as arsine or arsenic trihydride. Arsine and related alkyl compounds can also be generated by various fungi from arsenical wood preservatives (Richardson 1978).

2.4 Group V/Vb of the periodic table comprises in sequence nitrogen, phosphorus, arsenic and antimony and it was not therefore surprising that *S. brevicaulis* should form trihydrides of both nitrogen and arsenic, but it was surprising that there seemed to be no reports in the literature of similar generation of the trihydride phosphine from the intermediate element phosphorus and perhaps also similar generation of stibine from antimony. The stability of the trihydrides varies from ammonia which is stabel to bismuth trihydride which is unstable, rapidly oxidising in air. Less volatile alkyl compounds are also generated; it has been suggested that Gosio's arsenic was trimethylarsine rather than arsine but this may be an indication of the difficulties involved in identifying arsine rather than an authoritative indication that it is not generated (Challenger 1945; Cullen & Reimer 1989).

2.5 Richardson observed that the microbial infections on used mattresses always included *S. brevicaulis*, as well as many other fungi and bacteria which were known to be pathenogenic or known to be associated with generation of spores and mites prompting allergic reactions such as asthma; Richardson recommended investigation of the health risks associated with these organisms (Gravesen 1979; Holmberg & Kallings 1980; Sundin 1983; Anon. 1984; Barr et al 1985; Holmberg 1985; Croft et al 1986; Milberg 1987; Richardson 1991a). *S. brevicalis* i*u*nfections were concentrated in areas affected by the warmth and perspiration of the sleeping infant, development of this organism being prompted apparently by the presence of nitrogen compounds in the perspiration. *S. brevicaulis* was not only found on PVC cot mattress coverings but also on cotton, polyester and other covering fabrics and on the foams which are covered only by nets in some modern vented mattresses. Pink staining was frequently observed, sometimes as an outline of the body of a sleeping infant, when the affected materials contained phosphorus which prompts pink pigmentation in *S. brevicaulis.*

2.6 Richardson observed that *S. brevicaulis* infections in samples of mattress materials were always invisible but they could be detected by staining sections or by placing small pieces on a nitrogen-rich medium (malt and soya flower agar) on Petri dish plates, a medium that encouraged the spread of this fungus from the mattress samples onto the plate so that it could be readily identified; the fungus is polymorphic and a nitrogen-rich medium also prompts the fungus to change from the normal hyphal or filamentous form to a slime form which is often incorrectly identified as a contaminant bacteria or yeast. Other researchers who have attempted to replicate the Richardson investigations have encountered difficulties: the International Mycological Institute, who published the original papers describing dimorphism in *S. Brevicailis*, were unable to find this infection consistently on used mattress sample, and suggested that there was no evidence of dimorphism for this species, although it is possible that the organism is actually trimorphic with a third form involved in the infection within the structure of PVC fabric (Morton & Smith 1963; Onions 1966; Kelley et al 1992). Polymorphism exists when a micro-organism is found in different structural forms which may have been identified at times as different organisms, changing from one form to another, and reverting, when stressed in different ways, usually through transfer onto different culture media.

Gases generated from these cultures were identified using the Gutzeit method involving silver nitrate and mercuric bromide (or chloride) papers secured over the edges of the Petri dishes. These trihydride gases are reducing agents and eventually cause darkening of the silver nitrate but, before this darkening develops, phosphine causes a bright yellow colouration whilst arsine and stibine cause a pink or brown colouration; the mercuric bromide paper enables the latter gases to be distinguished as arsine causes a yellow to red colouration but phosphine and stibine cause no colour change. The related alkyl gases are not strong reducing agents but they cause similar but fainter colourations. An incubation temperature of about 22°C for these tests ensured that an antimony reaction indicated that only the trihydride stibine (BP -17°C) was present as the alkyl compounds are not volatile at that temperature, and arsenic and phosphorus reactions indicated that the trihydrides phosphine (BP -87°C) and arsine (BP -55°C) were most likely to be present, although theoretically the methyldihydride compounds might also be present. At normal cot mattress temperatures of about 37 °C the methyldihydride compound of antimony is also volatile, as well as the dimethylhydride and ethyldihydride compounds of phosphorus and arsenic. Doubts over the identity of the generated gases were prompted by reports which suggested that only alkyl compounds of arsenic are generated by biodeterioration, although it was not established that the trihydride was not also generated (Challenger et al 1933; Challenger 1945; Brahman & Foreback 1973; Cullen & Reimer 1989). The distinction between

trihydrides and related alkyl compounds is actually irrelevant as all the compounds are toxic with similar poisoning actions.

2.8 Richardson obtained blood samples from six SIDS victims. Antimony levels were 2.8, 4.8, 1.9, 1,9, 1,0 and 0,9 ng/ml; the three highest values weere associated with mattresses which were generating stibines. Normal antimony levels are 0.7 to 3.0 ng/ml in adults but less than 0.85 ng/ml in infants, so that there was an increase in blood antimony of about 2.0 ng/ml on the three highest results (Ward 1990). Analysis was limited to antimony because the known comparative toxicities of arsine and phosphine suggest that poisoning might increase arsenic and phosphorus levels in the blood by about 1.0 and 6.0 ng/ml respectively, but such increases would be undetectable with normal arsenic levels of 2.0 to 5.0 ng/ml and much higher phosphorus levels; the mattresses associated with the three lowest antimony values were generating phophines.

2.9 Polyvinyl chloride (PVC) cot mattress covers vary in composition but typically contain 55 to 60% PVC polymer and 30 to 35% plasticiser with 5 to 12% titanium dioxide and other pigments including antimony dioxide. Phosphate plasticisers and antimony trioxide have been used for many years to improve fire resistance, most fabrics containing either a phosphate plasticiser or antimony trioxide, although some contain both components. The concentrations of these fire retardants increased progressively for many years, particularly in England and Wales in 1985-87 in preparation for the introduction of the Furniture and Furnishings (Fire) (Safety) Regulations 1988 which prompted increases in the typical concentrations of phosphate plasticiser from 8 to 12% and of antimony trioxide from 1 to 4.5%. These regulations do not actually apply to mattresses, although all fillings must be fire resistant as they may be used in other furnishings, and the use of fire retardants in cot mattress coverings was adopted by manufacturers through ignorance of the requirements, a wish to adopt prudent precautions, or a wish to offer a product that appeared to be safer, even though cot mattresses are never the primary source of a fire as they are covered by bedclothes in normal use. Casualties through fires associated with bedding are extremely rare in infants; in the United Kingdom there are about 100 casualties annually up to five years old and for many years these included about five fatalities, but fatalities have increases to about fifteen since about 1985. Most of these fatalities involve toxic fumes rather than burns; the use of antimony trioxide in PVC causes the generation in fire of antimony trichloride, an effective flame suppressant which is also very toxic.

2.10 Phosphate plasticisers are generally triarylphosphates such as trixylylphosphate and tricresylphosphate. Biodeterioration of the plasticiser component in PVC particularly by *Aspergillus niger* and *Streptomyces rubrireticuli* has been extensively reported, but toxic gas generation through biodeterioration of components containing phosphorus, arsenic or antimony has not been previously considered (Klausmeier 1961, 1966, 1972; Yeager 1962, 1968). Antimony trioxide is common in PVC as a fire retardent as previously stated but it may contain up to 0.4% arsenic, and arsenic may also be present as OBPA preservative, although this preservative is not common in cot mattresses in the British Isles.

2.11 Cotton, polyester, polypropylene and other woven fabrics used for cot mattress coverings often contain fire retardant components or are treated with fire retardants of various types such as ammonium phosphates and chlorophosphates. Boron compounds are sometimes used, although they are not yet common in the British Isles. Filling materials may also incorporate various fire retardants, fibre fillings using the same fire retardants as for woven fabric coverings. Fire retardant foam fillings have only been generally introduced in England and Wales since about 1985 to conform with the Furniture and Furnishings (Fire) (Safety) Regulations 1988 and such foams are now often described as 'Combustion Modified'. Some foams contain fire retardants similar to those used in woven fabrics,

particularly chlorophosphate esters, sometimes with the addition of small amounts of antimony trioxide which improves fire retardancy by reaction with the chlorine content, but many combustion modified foams rely on graphite or melamine components to achieve sufficient fire resistance.

2.12 Although wool clothing, bedding and carpets are often 'proofed' against damage by moth and other insects with insecticide treatments, preservatives are not normally used on furnishing fabrics in the British Isles as other fabrics are not significantly at risk from insect attack and the risk of microbial deterioration is very small in a normal dry domestic environment. However, PVC intended for use in the sub-tropics and tropics is sometimes protected from termite and microbial attack using OBPA, an arsenical biocide 10,10'-oxybisphenoxyarsine, and in some countries such as Japan boron compounds are used which function as fire retardants as well as preservatives against microbial deterioration; boron compounds are now being used to an increasing extent in the British Isles.

2.13 The presence of phosphorus, arsenic and antimony compounds in mattress materials can be directly related to SIDS rates. In Japan where SIDS was unknown until recently, traditional infant mattresses are futons manufacturered from cotton alone and do not contain any of these elements; boron compounds are used both as fire retardants and preservatives. In recent years the SIDS rate in Japan has progressively increased from less than 0.1 to about 0.4 per 1,000 births, similar to the increase that occurred in England and Wales in 1950-55. In Japan the increase seems to be asociated with the progressive adoption of western-style child care practices, including the replacement of futons. The progressive increase in the SIDS rate in England and Wales eventually stabilized at about 2.0 in per 1,000 births in 1980, but later increased to a new level of about 2.3 in 1986-88 when use of fire retardents increased in preparation for the introduction of the Furniture and Furnishings (Fire) (Safety) Regulations 1988. SIDS rates are higher, typically about 4.0, where arsenical preservatives are used such as OBPA, and these rates increase even further where fire retardents based on phosphorus and antimony compounds are used in addition to arsenical preservatives; the SIDS rate amongst British Army families was about 5.8 in 1988 because they used issue mattresses which contained both fire retardents and OBPA preservative at that time; this compares with 2.5 for all SIDS in England and Wales, but the correct comparison should be with infants of married parents at 1.55 The old type of service mattresses are still in use by Royal Air Force families who still suffer exceptionally high SIDS rates. Lamb fleeces are often used as cot mattresses in Australia and New Zealand, and result in exceptionally high SIDS rates up to 20.0 in some areas, apparently where the wool contains arsenic or antimony acquired through sheep feeding on grass contaminated with soil containing these elements.

2.14 Absorption by inhalation is not the only route of entry for the toxic gases as they can also be absorbed through the skin. The rate of absorption can be substantially increased if some sterilization and detergent treatments are used for infant clothes, nappies and bedclothes; SIDS rates reduced sharply from about 8.5 per 1,000 births to less than 2.0 in Southland in New Zealand when mothers were advised to rinse farics instead of leaving them unrinsed as recommended by the manufacturers for some products (Sprott 1993).

2.15 Phosphorus in plasticisers and fire retardants, arsenic present as impurities in antimony trioxide and in the biocide OBPA, and antimony in antimony trioxide fire retardants are the sources of the extremely toxic phosphines, arsines and stibines that have been identified, but these gases can only be generated by an organism such as *S. brevicaulis* if sufficient energy is available. Generally the micro-organism must have access to an hydrocarbon, although some energy can also be obtained by deterioration of nitrogen or even phosphorus compounds. In PVC the chlorine groups provide some protection for the

PVC polymer itself and the plasticiser therefore forms the main nutrient in biodeterioration, but if nitrogen compounds are present from perspiration, vomit or urine, or as ammonium phosphate or melamine fire retardant components, development of *S. brevicaulis* is particularly encouraged. This organism will convert nitrogen compounds to the trihydride ammonia which is also toxic but disperses readily as it is lighter than air but, if sufficient energy is available, it will also generate phosphines, arsine or stibine from any phosphorus, arsenic or antimony compounds that are present. Generation of these gases is therefore usually associated with deterioration of the plasticiser and progressive development of brittleness, particularly where development of this fungus is encouraged by the warmth and perspiration of the infant. On other fabrics and fillings a variety of micro-organisms will develop on areas affected by perspiration, dribble or vomit but including *S. brevicaulis* so that again phosphines, arsines or stibines may be generated if suitable sources of phosphorus, arsenic and antimony are accessible to the organism.

2.16 Mattress biodeterioration can only occur if sufficient moisture is present within the affected materials. The air around an infant in a cot is saturated with moisture and the relative humidity of the air is therefore 100%. There is a temperature gradient between the interior and exterior of the cot through the bedding and mattress materials, and diffusion of this saturated air towards the exterior will result in cooling and interstitial condensation within these materials, providing the moisture which is necessary for the development of microbial infections and mattress biodeterioration (Richardson 1991c). Interstitial condensation is more severe if the saturated internal air is at a higher temperature, as in infant hyperthermia prompted by viral or bacterial infection or overwrapping.

Toxicology of Group V/Vb trihydrides and related compounds

2.17 Nitrogen, phosphorus, arsenic, antimony and bismuth are elements of increasing atomic weight which form Group V/Vb in the periodic classification of the elements. It is well known that many micro-organisms are able to convert nitrogen compounds such as protein into the trihydride ammonia and related alkyl compounds or amines. This ability to generate trihydrides is particularly well developed in the fungus *Scopulariopsis brevicaulis* which is able to utilize nitrogen from a wide variety of sources including nitrate and ammonium compounds, as well as urea, proteins and nitrogen polymers such as melamine. *S. brevicaulis* and several other organisms can similarly generate phosphine, arsine, stibine and related alkyl compounds from substrates containing phosphorus, arsenic and antimony, although it seems that *S. brevicaulis* is most active in this respect if nitrogen compounds are also present, presumably because they stimulate the enzymatic processes that are involved. Generation of these hydrides and related alkyl compounds in the cot environment introduces a toxic hazard which varies according to the compounds that are involved.

2.18 Ammonia, phosphine, arsine and stibine are gases with densities of 0.65, 1.17, 2.68 and 4.29 relative to air. Mothers are usually aware of ammonia generation as the pungent odour and low density mean that it is readily detected above the cot, but phosphine, arsine and stibine are denser than air and virtually odourless, and accumulate on top of the mattress, particularly if the infant is well wrapped; stibine is particularily dense and also unstable as it oxidises rapidly in air so that it is only present just above the mattress surface and only infants in the prone position are at risk, but phosphine is only slightly denser than air and is stable so that it can represent a risk in any position, although the risk is likely to be less in the supine position. The alkyl compounds of phosphorus, arsenic and antimony are denser than the trihydrides but at normal cot temperatures of 37 °C only the methyldihydride compounds of all three elements and the dimethylhydride and ethyldihydride compounds of phosphorus and arsenic are volatile. Whilst phosphine, arsine and stibine

are colourless and odourless, their associated alkyl compounds have distinctive odours which are often attributed to the trihydrides themselves. Thus the standard toxicological literature usually states that phosphine has a 'dead fish' or 'garlic' odour, arsine is more distinctly 'garlic', and stibine odour is usually described only as 'very unpleasant'. The threshold limit values (occupational exposure limits assuming 8 hours exposure) for phosphine, arsine and stibine are usually quoted as 0.3, 0.05 and 0.1 ppm respectively, indicating extreme toxicity; these gases are about 300, 2,000 and 1,000 times more toxic than carbon monoxide which has a TLV of 100 ppm (Anon. 1989; Anon. 1990). The garlic odour associated with arsine is only usually detectable at concentrations well in excess of the TLV.

2.19 It has been reported that it is difficult to confirm that an infant has absorbed sufficient phosphine, arsine or stibine to cause death (Richardson 1991a, b). Blood samples from six SIDS victims were found to have antimony levels of about 2.8, 4.8, 1.9 1.0, 1.0, and 0.9 ng/ml respectively compared with normal ambient levels of 0.7 to 3.0 ng/ml in adults but less than 0.85 ng/ml in infants (Ward 1990). These results suggest that the blood antimony level was increased by about 2.0 ng/ml in the first three samples by stibine poisoning, tests on the PVC components of the mattrresses involved indicating stibine generation, although the normal maximum level of 0.9 ng/ml in infants may include some contribution from mattress stibine in non-fatal situations. The mattresses for the other blood samples were found to be generating phophine. The known comparative toxicities of arsine and phosphine suggest that poisoning might increase arsenic and phosphorus levels in the blood by about 1.0 and 6.0 ng/ml respectively but such increases are undetectable in the presence of normal arsenic levels of 2.0 to 5.0 ng/ml and much higher phosphorus. levels. These calculations would suggest that lethal doses of phosphine, arsine and stibine in infants might be 60, 10 and 20 ng/Kg body weight respectively. Mixtures of gases are probably additive in effect because of their identical mode of action. These gases are eliminated by excretion in urine and deposition in the keratin in hair, and significant toxic effects only develop when the rate of gas absorption exceeds the rate of elimination; hyperthermia in an infant increases the rate of gas generation from mattress materials (Richardson 1991a, 1994). Antimony levels in urine can be used to monitor short term exposure in infants; indicating the exposure shortly before test, and antimony levels in hair and nails can be used to monitor chronic exposure; arsenic may be checked in the same way, but normal phosphorus levels in urine are too high for this element to be monitored. Analysis of the mother’s hair can be used to establish levels for the normal domestic environment, but levels in infants are always much higher if they have been sleeping several months prior to test on mattresses containing arsenic or antimony compounds and which have been in use for at least several months so that natural *S. Brevicaulis* infection has become established.

2.20 The typical symptoms of arsine poisoning in adults are well known (Hunter 1936; Josephson et al 1951; Doig 1958; Teitelbaum & Kier 1969; Hocker & Bradshaw 1970; Cooper 1974; Pinto 1976; Kleinfeld 1980; Selzer & Ancel 1983; Polson et al 1983; Dreisbach 1983; Tver & Anderson 1986; Plunkett 1987; Moorman et al 1987; Hong et al 1989; Rosenthal et al 1989). Poisoning by phosphine and stibine is not so frequently reported and is not described in such detail in the literature but they are exceedingly poisonous gases with the same mode of action and symptoms as arsine; the main differences arise only through differences in density and toxicity (Fairhall 1947; Cooper 1974; Wilson et al 1980; Dreisbach 1983; Polson et al 1983; Tver & Anderson 1986; Plunkett 1987; Misra et al 1988). Phosphine, arsine and stibine are much more toxic than other phosphorus, arsenic and antimony compounds. Poisoning by these gases is usually diagnosed in adults through erythrocyte haemolysis and Heinz body formation, but

haemolysis only develops 6 to 24 hours after severe acute exposure and such symptoms are not normally associated with SIDS. If phosphine, arsine and stibine are a cause of SIDS, death must result from some other action before erythrocyte haemolysis develops, either because infant erythrocytes are more resistent to haemolysis or because infants are more susceptible to some other poisoning action. Phosphine is the simplest phophorus-based nerve poison and is used commercially as a fumigant insecticide for grain; there are several reports of accidents involving phosphine and arsine poisoning with child fatalities but only illness in adults (Gosio 1892, 1893, 1897; Sanger 1894a, 1894b; Schmidt 1899; Anon 1932; Thom & Raper 1932; Wilson et al 1980).

2.21 Poisoning by phosphine, arsine and stibine results in the accumulation in the blood of phosphonium, arsonium and stibonium ions which are weak bases and absorb carbon dioxide; they can change the tonicity or osmotic pressure of the blood in this way, a process that probably accounts for the erythrocyte haemolysis observed in adults, although lysis may be associated with chemical modification of the haemoglobin which may contribute to the observed hypoxia in SIDS; certainly arsenic has been identified in erythrocytes as dimethylarsinate (Fowler & Weisberg 1974; Cullen & Reimer 1989). The removal of carbon dioxide from the blood will also reduce stimulation of respiration, through the respiratory centre which is the carotid sinus in infants rather than in the medulla as in adults, and it is not therefore surprising that suppression of respiration is sometimes reported as a feature of poisoning by these gases, although it is not known whether carbon dioxide neutralisation is involved or a direct action of the toxic trihydride gases on the chemoreceptors associated with respiratory control. Phosphine, arsine and stibine are also reported to cause depression of the central nervous system through an anticholinesterase action which would cause cardiac inhibition and vasodilation in infants through progressive accumulation of acetylcholine from the vagus nerve, a mechanism that would be completely consistent with SIDS and which would also explain certain unusual observations such as death a few minutes after lifting the infant from the cot (Cooper 1974; Kleinfeld 1980; Rognum et al 1988; Berry 1992; Matturi 1992). Cardiac failure through excessive vagus acetylcholine has been suggested as a cause of SIDS and has been attributed to vagus nerve dysfunction, although the symptoms are identical with anticholinesterase poisoning (Farber et al 1983; Greenwald 1984). The anticholinesterase action of organophosphorus pesticides and chemical warfare agents is well known and congestive cardiac failure is reported for phosphine poisoning, but these gases may also interfere with other enzyme systems, such as those involved in glycogen and fatty acid metabolism, and in muscle contraction (Klimmer 1969). Phosphonium, arsonium and stibonium cations may also condense onto blood glucose units in the 1 and 6 positions, preventing glucose utilisation and causing irritation of the central nervous system followed eventually by death; organotin and organolead cations have a similar action (Richardson 1969, 1988).

2.22 If poisoning by phosphines, arsines and stibines is the primary cause of SIDS, the risk can be completely avoided only by eliminating phosphorus, arsenic and antimony from mattress materials. However, whilst most infants are apparently exposed to this poisoning in western-style communities, as well as in Australia and New Zealand where fleeces containing arsenic and antimony are used as cot mattresses, other contributory factors will decide whether an infant is unaffected or suffers irritability, illness or death. The rate of gas generation will depend on the activity of the *S. brevicaulis* infection. SIDS is almost always associated with previously used mattresses in which the infection has become well established during previous use and reactivated by the new use, so that first children are least at risk as they are more likely to use new mattresses, and lower social class groups are more at risk because they are more likely to use previously used mattresses (Richardson

1990, 1991a,d). SIDS is mainly associated with infants older than 1 month as it usually takes several weeks to reactivate an infection on a previously used mattress to a sufficient extent for it to generate significant amounts of toxic gas, and deaths at less then 1 month generally occur on mattresses which are in current use by an older infant, typically when a family with a very young infant is visiting friends or relatives. SIDS is unusual at ages of more than 5 months and very rare at ages of more than 14 months; the first sign of poisoning by these gases is a headache which causes irritability, an older and stronger infant dislodging the bedding and dispersing the gas, SIDS cases at more than 5 months involving weaker infants, generally those that are underweight or unwell. It has been suggested that bacterial and viral infections increase the SIDS risk but higher temperatures caused by these infections will increase the rate of toxic gas generation and analgesic medication will suppress the headache which warns of poisoning by these gases, reducing irritability and increasing the risk of death.

2.23 Phosphines, arsines and particularly stibines are heavier than air and accumulate on top of the mattress. The SIDS risk is highest in the prone or face down position which involves maximum exposure to the heaviest gas stibine which is also unstable, although a few cases can still occur in the supine of face up position, particularly on mattresses containing phosphorus compounds as phosphine is only slightly heavier than air. Overwrapping traps gas around the infant but also results in hyperthermia or overheating, prompting increased fungal activity and gas generation; the rate of gas generation increases about 20 times if the cot temperature increases from 37°C to an hyperthermic temperature of about 42°C (Richardson 1991a, 1994). Hyperthermia can also be aggravated by mild and otherwise insignificant viral or bacterial infections (Milner & Ruggins 1989; Berry 1992; Essery et al 1994; Murrell et al 1994). Hyperthermia through overwrapping is more likely in male infants because of their higher metabolic rate; the SIDS rate for males is about 55% higher than for females. In twins it has been observed that if one is a SIDS victim the other may suffer from haemorrhagic shock encephalopathy syndrome (Trounce et al 1991). It is probable that both infants are similarly affected by hyperthermia, that one infant was on a previously used mattress suffering active biodeterioration and toxic gas generation which caused death diagnosed as SIDS, whilst the survivor was affected by intensifying hyperthermia; the symptoms of HSES are similar to those of heatstroke (Bacon 1991).

2.24 Recommendations to parents that the prone or face down sleeping position should be avoided can significantly reduce the SIDS risk; in the Netherlands, New Zealand and the State of Victoria in Australia this precaution alone has reduced the SIDS rate by about 40% (Engelberts & de Jonge 1990). In the United Kingfdom a local recommendation in the Avon area achieved a similar reduction (Flemming et al 1990). The Department of Health *Back to Sleep* campaign introduced in November 1991 recommended that the prone position and overwrapping should be avoided was also effective in reducing the SIDS rate in England and Wales, although a steady decrease commenced more than two years earlier following recommendations that a new mattress should be provided for every new infant or old mattresses should be covered to isolate the infant from the mattress materials (Richardson 1990). However, these precautions will only remain effective whilst parents are continuously reminded, and the SlDS risk can only be permanently reduced by totally prohibiting mattress materials containing phosphorus, arsenic or antimony compounds.

The Turner Report

2.25 In England the Department of Health established an expert working group in March 1990 to investigate the Richardson hypothesis that SIDS is caused by gaseous phosphine, arsine, stibine and related alkyl compounds generated by biodeterioration of cot matress materials.

Their report was issued on 12 June 1991 (Anon. 1991).

2.26 The group instructed the Laboratory of the Government Chemist and the International Mycological Institute to repeat the investigations on which the hypothesis was based, but the LGC results were considered to be inconclusive; they had modified the experimental methods and they were unable to consistently detect arsenic gases even when they were expected to be generated from samples spiked with arsenic, and they detected an antimony gas which could only be present if the hypothesis is correct. The group reported that the generation of phosphine was unlikely on theoretical grounds, whereas the established generation of ammonia and arsine actually suggests that it would be surprising if phosphine was not similarly generated. The group considered that poisoning by phosphine, arsine, stibine or related toxic gases was unlikely in SIDS as erythrocyte haemolysis, the most common symptom of poisoning reported in adults, had not been observed, ignoring the possibility that infants may die before the development of haemolysis because they are more sensitive than adults to some other poisoning action or because infant erythrocytes, which are physiologically different from adult erythrocytes, may be more resistant to haemolysis. The group did not commission any investigations which might have confirmed that SIDS may be caused by poisoning by the toxic gases that had been reported, despite reports of blood analyses which indicated high antimony levels in SIDS victims who had died on mattresses apparently generating antimony gases. The group reported but ignored the significant reduction in the SIDS rate in England and Wales that had followed recommendations that new mattresses should be provided for every new child (or old mattresses should be covered with polythene to isolate the child from the mattress materials) and the group did not even report the much larger decreases that occurred in 1990, even though these changes were apparent well before the report was published in June 1991.

2.27 It is not surprising that the group reported that the hypothesis was unproven through lack of any independent supporting data as the group ignored any data that was provided and avoided any investigations that might have confirmed the hypothesis. However, the group recommended that the potential toxicity of additives in mattress materials and their breakdown products should be investigated, emphasizing the possible significance of arsenic contamination of the antimony trioxide which is used as a fire retardant additive and the risk of formation of toxic volatile compounds. The group recommended that the hazards associated with microbial contamination should also be investigated.

2.28 It seems that these recommendations were not implemented by the Department of Health or by the Department of Trade and Industry which is responsible for safety problems involving cot mattresses.

Die Cook Reports

2.29 Der plötzliche Kindstod blieb weiterhin ein Thema der öffentlichen Besorgnis. Die Betonung auf Vermeidung der Bauchlage und Überwärmung war schwer zu verstehen; während diese Praktiken nicht wünschenswert erschienen, sah es nicht so aus, als hätten sie während der ersten Hälfte des zwanzigsten Jahrhunderts eine bedeutsame Anzahl von Kindstodesfällen verursacht. Naturwissenschaftliche und medizinische Forscher blieben über die ins Auge fallenden Widersprüche und Forschungsergebnisse ratlos und bestürzt, und diese unglückliche Situation rief bald das Interesse der Medienforscher wach. 1994 reichte Joan Shenton von der *Meditel* in Zusammenarbeit mit Roger Lavander dem *Central Television* Vorschläge für ein Programm ein, das später die Basis von zwei Programmen des *Cook Report* wurde, die am 17. November und am 1. Dezember 1994 ausgestrahlt

wurden. Während diese Programme gegenüber den inadequaten Untersuchungen der Turner Gruppe kritisch waren, gaben sie dem *Robens Institute* und den *Rooney Laboratories Limited* neue Untersuchungen in Auftrag, zu denen die Analyse von Geweben verstorbener Babies, Analysen von Matratzenteilen und Analysen von Haaren lebender Babies gehörten, dies im Bemühen um die Feststellung ob die Babies Antimon aus den Matratzen in Gasform absorbierten. Unter den Umständen, in denen das wahrscheinlichste Gas das extrem toxische Stibin war, lag die Betonung dieser Untersuchungen auf Antimon, da es in der Umwelt normalerweise selten vorkommt und in Körpergeweben nur in geringen Mengen gefunden wird, so dass die Rückstände einer Stibinvergiftung aufgedeckt werden können, während die Rückstände einer Phosphin- oder Arsinvergiftung wegen der natürlicherweise hohen Konzentrationen dieser Elemente in Geweben nicht nachgewiesen werden können.

2.30 Zu den ersten Gewebsanalysen im *Robens Institute* gehörten Serum- und Leberproben von 53 Kindstodesfällen. Einige Proben hatten einen extrem hohen Antimongehalt: alle diese Proben stammten von Babies, die als plötzlicher Kindstod diagnostiziert waren. Babies die durch andere Ursachen gestorben waren, hatten einen niedrigen oder meist unbestimmbaren Antimongehalt. Auch einige SIDS-Opfer hatten niedrige Antimonwerte: es ist möglich, dass diese Opfer einer Phosphin- oder vielleicht auch Arsinvergiftung waren; einige Kindermatratzen, die an Wehrdienst-Familien abgegeben werden, enthalten Arsen woraus Arsine generiert werden können. Wo ein Vergleich mit dazugehörigen Matratzen mit diesen Proben und anderen, die später verfügbar waren, durchgeführt werden konnte, standen hohe Antimonwerte in Geweben immer in Zusammenhang mit Antimonvorkommen in den Matratzen, auf denen die Kinder geschlafen hatten; nachfolgende mikrobiologische Tests an den gleichen Matratzen zeigten immer, dass sie mit *Scopulariopsis brevicaulis* infiziert waren und bei Inkubation Stibin generierten. In diesem Zusammenhang soll man wissen, dass hohe Antimonwerte in der Leber Anzeichen einer chronischen Stibinbelastung sind, während niedrige Leberwerte Anzeichen eines akkuten Vergiftungsfalles sind, manchmal durch den Wechsel aus dem normalen Bett in ein anderes, das in täglichem Gebrauch durch ein älteres Kind stand. Der in Beziehung zu dieser Kette von Antimon aus der Matratze über Gase in das Blut und Gewebe wesentliche Gesichtspunkt ist, dass Antimon in der Umwelt außerordentlich selten ist und bei Kindern in viel niedrigeren Konzentrationen gefunden werden sollte als bei Erwachsenen. Analysen von Haarproben bei Untersuchungen in Gemeinden zeigten, dass der Antimongehalt bei Babies oft viel höher war als der ihrer Mütter, was zeigt, dass keine ungewöhnlich hohe Belastung im allgemeinen häuslichen Milieu vorlag, sondern nur in der speziellen Umgebung des Kindes. In allen Fällen von hohen Antimonwerten im Haar fand man einen Zusammenhang mit Antimon in Kinderbett- oder Kinderwagenmatratzen.

2.31 Die *Cook Report* Programme waren auch der Anlass für einige Kommentare von Eltern und Beratern in Bezug auf Fälle von Apnoe und anscheinenden nahezu-Fällen von SIDS, von denen einige als Erstickungs-Versuche der Eltern oder Kinderbetreuer gedeutet wurden. Ereignis-Monitore zeigen gewöhnlich vor der Apnoe eine progressive Verlangsamung der Herzfrequenz, die mit einer Anticholinesterase-Vergiftung durch in den Matratzen generiertes Phosphin, Arsin oder Stibin übereinstimmt, aber manchmal steht die Apnoe in Zusammenhang mit einer Beschleunigung der Herzfrequenz, die höchstwahrscheinlich in Zusammenhang mit einer respiratorischen Obstruktion, einer vielleicht absichtlichen oder akzidentellen Erstickung, steht, obwohl ein Bronchialoedem oder Asthma ebenso die Ursache sein können (Schechtman et al. 1991; Berry 1992; Matturi et al.1992; Pincus et al. 1993; Hoppenbrouwers et al. 1993; Keens & Ward 1993; Robinson 1994).

2.32 Nach Berichten über Wehrdienst-Familien leiden diese an einer sehr hohen SIDS-Rate, aber nach Antworten auf den *Cook Report* sieht es so aus, dass sie außerdem an einer ungewöhnlich hohen Anzahl von Apnoe und nahezu-Fällen von SIDS leiden, wahrscheinlich weil in den diesen Wehrdienstfamilien ausgehändigten Matratzen, wie schon berichtet, Arsenverbindungen verwendet werden, und Arsin, das durch Biodeterioration dieser Verbindungen generiert wird, stellt das größte Risiko einer derartigen Vergiftung dar. Die Britische Armee wurde von Richardson vor der Gefahr, die in Zusammenhang mit der Verwendung des arsenhaltigen Konservierungsmittels OBPA in Kindermatratzen steht, gewarnt und ersetzte ihren Vorrat vor einigen Jahren. Analysen der Rooney Laboratorien für den *Cook Report* zeigen, dass in den gegenwärtig gebrauchten Armee-Matratzen kein Arsen enthalten ist, aber in fünf Matratzen des früheren, inzwischen zurückgezogenen, Matratzentyps fand man Arsen in den entsprechenden Konzentrationen. Dieser Wechsel der Matratzen hat zu einem wesentlichen Rückgang der SIDS-Fälle in Familien der Britischen Armee geführt. Die Britische Luftwaffe hat jedoch die älteren Matratzen beibehalten und hat immer noch eine ungewöhnlich hohe SIDS-Rate bei ihren Wehrdienst-Familien, ebenso wie einen hohen Anteil an Apnoe und nahezu-SIDS-Fällen. Die Situation bei den Familien der Königlichen Marine ist nicht bekannt.

2.33 Die ursprünglichen Richardson Berichte enthielten den zusätzlichen Kommentar, dass PVC-umhüllte Matratzen ideal erschienen, weil sie leicht zu reinigen und hygienisch, sowie sicher seien, sofern sie keine Phosphor-, Arsen- oder Antimonverbindungen enthielten. Im Gegensatz dazu gab es eine zunehmende Umstellung in Richtung von Matratzen mit unbedecktem Schaumstoff, bei denen ein Teil oder die gesamte Schaumstoff-Füllung nicht oder nur durch ein Netz oder ein dünnes Gewebe bedeckt ist, dies wahrscheinlich im Glauben, dass der Gebrauch dieser durchlässigen Matratzen die Gefahr einer Asphyxie durch Inhalation von Erbrochenem vermindert, obwohl es keinen Beweis dafür gibt, dass die Inhalation von Erbrochenem jemals eine signifikante Ursache von Todesfällen bei Babies war. Die ursprüngliche Untersuchung von Wiegenmatratzen von Richardson hat gezeigt, dass diese unbedeckten Schaumstoffbereiche schwere Infektionen durch eine große Anzahl von Organismen unterstützen, von denen viele Sporen produzieren, von denen man weiß, dass sie in Zusammenhang mit der Entwicklung von Asthma bei empfindlichen Individuen stehen. Die Fungus-Infektion unterstützt außerdem eine schwere Verseuchung mit Milben, die ebenfalls oft in Zusammenhang mit Asthma stehen. Es wurde empfohlen, Matratzen mit unbedecktem Schaumstoff zu vermeiden, die Hersteller haben allerdings nichts geändert. Nach dem zweiten *Cook Report* riefen aber viele Eltern an, um zu sagen, dass sie in Übereinstimmung mit den Empfehlungen des Programms zwei Wochen vorher ihre Matratzen mit Polyethylen umhüllt hatten und dass ihre Babies und Kleinkinder seitdem keine so schweren oder so häufigen Asthmaanfälle mehr gehabt haben und in vielen Fällen keine Behandlung mit Ventalin mehr brauchten.

3. SUDDEN INFANT DEATH SYNDROME

3.1 Sudden unexplained infant deaths first attracted attention in 1954 when Barrett reported a large increase in the unexpected deaths of apparently healthy infants and, as they occurred mainly in sleep, he suggested that these additional deaths should be described as cot deaths; in north America crib death is preferred. The death rate increased steadily and the cause remained unidentified despite intensifying research. It was observed that most but not all deaths occurred during sleep, but not all in sleeping quarters, and in 1969 Beckwith proposed at a conference in the USA that *The sudden death of any infant or young child which is unexpected by history, and in which a thorough post-mortem examination fails to demonstrate an adequate cause of death* should be described as sudden infant death syndrome (SIDS). This definition was adopted as code 798.0 under the International Classification of Diseases, and this new classification soon appeared in the mortality statistics for those countries in which SIDS is recognised.

3.2 SIDS rates continued to increase steadily, perhaps due to increasing recognition of SIDS with a corresponding reduction in other causes of death, but SIDS rates in some countries were too high to be explained in this way. One of the problems with SIDS is the frequent absence of any positive diagnosis; SIDS is, in effect, diagnosed by exclusion in the sense that it is unexpected in history and thorough necropsy fails to demonstrate an adequate cause, although there are now some pathological findings that are recognised as being characteristic of SIDS such as localized intrathoracic petechiae and extramedullary haemopoiesis in liver, these observations sugesting hypoxia (Berry 1992). The causes of SIDS remained unidentified, despite continuing investigative research, but a change in emphasis towards epidemiological studies achieved greater success in establishing the characteristic features of SIDS (Kelly & Shannon 1980; Kelly et al 1982; Golding et al 1985; Milner 1987; Southall et al 1987; Milner & Ruggins 1989). Since 1984 various precautions have been recommended to reduce the risk and SIDS rates are now decreasing in several countries as a result, but it remains difficult to distinguish between primary causes, contributory causes and resulting symptoms.

3.3 This review of SIDS research considers the various hypotheses that have been proposed and the ways in which they relate to both the established epidemiological features and the precautions that have achieved reductions in the SIDS rates, and the hypothesis that a primary cause of SIDS may be biogeneration of toxic gases from matresses containing phophorus, arsenic and antimony.

Epidemiology

3.4 SIDS rates increased steadily from about 1953 when this condition was first recognised as cot death to 1987, perhaps due to improved recognition and reporting. The SIDS rates were about 2 to 4 per 1,000 live births in 1985-88 in western Europe, north America and most other western-style countries, but the rates were very low and SIDS was not recognised in Russia, China, Japan, Thailand, India and parts of Africa (Golding et al 1985; Morris 1986; Becroft & Mitchell 1989; Gordon 1989). The SIDS rates in Hong Kong, and amongst infants of African or Asian origin in England and Wales, were intermediate, apparently indicating intermediate style communities (Lee et al 1989; Balarajan et al 1989). It was suggested that overcrowding in homes in Hong Kong might be an advantage by providing an infant with a continous stimulus, an hypothesis that might also explain the lower SIDS rate amongst infants of African and Asian origin in England and Wales, but this does not explain why SIDS is not recognised at all in so many countries (Lee et al 1989). Recently SIDS has been recognised in Japan and has now risen to about 0.4 per 1,000 births, coinciding with progessive abandonment of traditional child care practices with babies sleeping face up on cotton futons and wider adoption of western-style practices including

mattresses (Watanabe et al 1994).

3.5 Figure 1 shows the accumulative postneonatal deaths for England and Wales (OPCS Monitor DH3 93/2). In this diagram each cause of death is represented by the areas between the lines. The SIDS rate has increased steadily since 1970 when this cause of death was first officially recognised but has remained reasonably constant since about 1981. SIDS deaths prior to 1970 were included in one or more of the other groups, and the way in which this diagram is presented has prompted the suggestion that they were previously diagnosed as respiratory diseases. Whilst it is probably true that some sudden infant deaths wer diagnosed as unidentified respiratory problems and therefore included in this group, unexplained deaths would normally be included in the top 'other' group in this diagram. The progressive reduction in respiratory diseases can be attributed to improved antibiotics and can be seen in mortality rates in all age groups in most countries, including those in which SIDS is not recognized. A reduction in the 'other' group from about 1.3 prior to 1973 to 0.8 after 1976 can certainly be attributed to the introduction of the SIDS classification, but the steady increase in SIDS after 1976 without any proportionate redcution in the 'other' group indicates that SIDS rates have since been increasing, reaching a reaonable constant level in 1982-85, and then increasing to a slightly higher level in 1986-88. In 1989 there was a significant reduction in the infant mortality rate, due entirely to a substantial reduction in the SIDS rate, which continued in 1990. Figure 2 shows a diagram in which SIDS incorrectly classified under other causes of infant death have been estimated, and figure 3 shows the probable historical development of SIDS, estimated by incorporating the corrections deduced from figure 2. Figure 3 shows that the peak SIDS rate developed 1986-88, during a period when mattress manufacturers were incorporating the highest levels of phophorus and antimony fire retardants, prompted by the introduction of the Furniture and Furnishings (Fire) (Safety) Regulations 1988. The figure 3 also shows the sharp decrease in the SIDS rate which first developed in 1989, following recommendations by Richardson for the adoption of mattress precautions.

3.6 Seit vielen Jahren hat man festgestellt, dass die SIDS-Inzidenz von der Außentemperatur abhängig ist. Diese Temperatur wir am bequemsten durch den privaten Heizölverbrauch bestimmt (Frogatt et al 1971; Murphy & Campbell 1987; Hereward 1991; Richardson 1991a). Die Beziehung zwischen der SIDS-Inzidenz und diesem Maß für die Außentemperatur zeigt die Abbildung 4; die Abbildung zeigt auch, dass der kürzliche Rückgang der Todesfälle nicht auf eine Änderung der Wetterverhältnisse zurückzuführen ist. Veränderungen in der vierteljährlichen SIDS-Inzidenz können bequemer verfolgt werden wenn man die Inzidenz der Quartale in Prozent dieser Quartale in den Jahren 1986-88 ausdrück, wie in Abbildung 5. Einige der Änderungen seit der relativ stabilen Periode von 1986-88 kann man auf die Ereignisse beziehen, die die Kinderversorgung betroffen haben. Das Heizöl-, bzw. Außentemperatur-Diagramm der Abbildung 4 zeigt, dass es klimatische Veränderungen gab, insbesondere wärmeres Wetter als üblich in den ersten Quartalen 1989 und 1900, ignoriert man diese zwei Punkte allerdings, sieht man einen Rückgang (der SIDS-Inzidenz) der im dritten Quartal 1989 beginnt, der sich mit Ausnahme einer vorübergehenden Zunahme im dritten Quartal 1990 und in den zweiten und dritten Quartalen 1991 fortsetzt. Dieses Muster passt konsistent zu der Reaktion der Eltern auf die Empfehlung der Vorsorge in Bezug auf die Matratzen, und die temporären Unterbrechungen des Rückgangs fallen zusammen mit den Behauptungen des *Department of Health,* die nahe legten, dass eine Vorsorge in Bezug auf die Matratzen nicht nötig sei. Im November 1991 begann das *Department of Health* mit seiner *Schlaf auf dem Rücken*-Kampagne, in der empfohlen wurde, das Schlafen auf dem Bauch zu vermeiden. Erfahrungen mit ähnlichen Kampagnen in den Niederlanden und in Neuseeland ließen vermuten, das diese gut publizierte Empfehlung zu einer prompten Verminderung der SIDS-Inzidenz von etwa

40% führen sollte, wie die punktierte Linie in Abbildung 5 zeigt, während sich diese vorauszusehende Änderung aber durch den Rückgang auf die sehr niedrige Raten im vierten Quartal 1991 und ersten Quartal 1992 darstellt, ist klar, dass der Effekt dieser Kampagne des *Department of Health* auf einen progressiven Rückgang der Zahlen aufaddierte, der bereits gut etabliert war. Tatsächlich legen die Zahlen in den folgenden Quartalen von 1992 nahe, dass ein Effekt dieser Kampagne war, den progressiven Rückgang, der offensichtlich auf die Matratzen-Vorsorge zurückzuführen war, zu unterbrechen, obwohl man aus den Zahlen für 1993, die in der Presse bekannt aber nicht formell publiziert wurden, nicht ersehen kann, dass sich der stetige Rückgang fortgesetzt hat und die SIDS-Inzidenz jetzt nur noch etwa 12% der durchschnittlichen Inzidenzen für die Quartale 1986-88 beträgt. Das überrascht, da die *Schlaf auf dem Rücken*-Kampagne des *Department of Health* im Effekt die Kampagne in Bezug auf die Matratzen-Vorsorge völlig ausgelöscht hatte, und es irgend eine weitere Erklärung für den sich fortsetzenden Trend geben muss. Die Antworten der Hersteller im *Cook Report* haben dafür eine unerwartete aber offensichtliche und sehr willkommene Antwort gegeben: Die Hersteller von Kindermatratzen haben die Antimon- und Phosphoranteile, die als eine primäre Ursache von SIDS vermutet wurden, progressiv reduziert.

3.7 Detaillierte Untersuchungen der SIDS-Statistik für England und Wales zeigen an, dass das Risiko im Alter zwischen ein und fünf Monaten am höchsten ist, etwa 50% höher für Jungen als für Mädchen, und etwa 60% niedriger für erstgeborene Babies als für die folgenden; es gibt wenig Unterschiede in Bezug auf den sozialen Status für erstgeborene Babies, aber ein höheres Risiko für niedrigere soziale Klassen für die nachfolgenden Babies (Richardson 1991d). Verschiedene andere Faktoren sind identifiziert worden aber einige von ihnen kann man gruppieren; das höchste Risiko, zum Beispiel, hat ein frühgeborener Zwilling (oder Drilling) mit einem niedrigen Geburtgewicht, der an einer verlangsamten körperlichen Entwicklung leidet, eine Mutter hat, die raucht, und während der Schwangerschaft eine Anämie hatte, oder einer Mutter mit einer schlechten pränatalen Fürsorge, alle diese Faktoren aber führen in ihrer Tendenz zu Kindern mit einem niedrigen Gewicht und einer für ihr Alter verminderten Aktivität. Andere Faktoren, die man gruppieren kann sind junge Mütter, unverheiratete Mütter, Kinder aus Mehlingsgeburten, zweite oder nachfolgende Kinder, Armut der Eltern und Alkoholismus der Eltern, alles Faktoren, die vielleicht zu schlechter Fürsorge durch die Eltern aber auch zu einem niedrigen sozialen und ökonomischen Status führen, alle diese Faktoren führen, aber auch zu ökonomischen Bedingungen, die bedeuten, dass der Gebrauch einer neuen Matratze unwahrscheinlich ist (Richardson 1990, 1991a,d).

3.8 The SIDS rate in New Zealand of about 6 per 1,000 live births was high compared with other western-style communities, but the rate amongst caucasian infants was actually lower at 1.6 and the rate amongst Maori infants was exceptionally high at 11.5, although there has since been a significant reduction since the publicity recommending the avoidance of the prone sleeping position (Mitchell et al 1987; Mitchell et al 1994). A similar high SIDS rate was reported amongst aborigines in Australia, suggesting an ethnic susceptibility, perhaps a dietary factor, although it has also been suggested that these figures might actually indicate a geographical distribution with the lamb fleeces that are traditionally used as cot mattresses in Australasia containing these elements; recent information from New Zealand suggests a geographical distribution rather than an ethnic distribution as some of the highest SIDS rates were actually amongst caucasian families (Richardson 1991a, b; Sprott 1993).

3.9 In the Netherlands it was observed that the SIDS rate had increased from 0.46 per 1,000 in 1969-71 to about 1.31 after 1978, and it was thought that this increase might be

associated with a suggestion at a paediatric conference in 1971 that infants should sleep in the prone position (de Jonge et al 1989). It was recommended in 1987 that parents should avoid the prone position, and the SIDS rate dropped by about 40% from 1.13 in 1987 to 0.76 in 1988 (Engleberts & de Jonge 1990). Similar recommendations in New Zealand and the State of Victoria in Australia achieved similar reductions in the SIDS rate (Beal 1988; Mitchell Engelberts 1991). It was established in the Netherlands that the SIDS risk was about 2.2 times greater in infants that may be prone compared with those that are never prone, and 4,6 times greater in infants that are always prone, whilst in New Zealand the lateral position has been found to increase the risk 2.29 times and the prone position 7.44 times (Mitchell & Engelberts 1991). Recommendations in England in July 1990 that overwrapping and the prone position should be avoided have also contributed to a progressive decrease in the SIDS rate (from 3.7 to 1.8 in the Avon area involved in the experiment), although the decrease throughout England and Wales was first observed a year earlier following recommendations in June 1989 that a new mattress should be used for every new child or old mattresses should be covered with polythene sheet to isolate the infant from the mattress (Fleming et al 1990; Richardson 1990, 1991a, b, d. Berry 1991).

3.10 Es wurde auch nahe gelegt, dass die Bevorzugung der Rücken- eher als der Bauchlage in Japan und China für das offenbare Fehlen des plötzlichen Kindstodes in diesen Ländern verantwortlich sein könnte, aber die Wahl der Schlafposition beeinflusst nur die Inzidenz, ohne den plötzlichen Kindstod zu eliminieren, und die Bauchlage wurde auf den Britischen Inseln gewählt, bevor noch SIDS 1952 erkannt worden ist, und wird in Japan in zunehmendem Maße gewählt, ohne dass SIDS ein größeres Problem geworden ist (Lee et al 1989). Die Säuglingssterblichkeit in Japan zu dieser Zeit lag bei etwa 5.2 pro 1.000 Lebendgeborene, im Vergleich zu 8.6 für England und Wales 1986-88. Die niedrigere Inzidenz in Japan wird nahezu vollkommen durch das Fehlen des plötzlichen Kindstodes erklärt, das in England und Wales etwa 2.3 betrug; der größte einzelne Anteil in Japan waren kongenitale Abnormitäten mit 1.7% (zweimal so viel wie in England und Wales mit 0.8) aber selbst das war viel zu wenig um einen nicht erkannten plötzlichen Kindstod zu verbergen. Man muss daher daraus schließen, dass der plötzliche Kindstod in Japan zu dieser Zeit keine wesentliche Rolle spielte. Diese Untersuchungen legen nahe, dass die wahrscheinliche Ursache für diese Unterschiede die Tatsache ist, dass die traditionellen Futons, die zu dieser Zeit von japanischen Kindern benutzt wurden, frei von den Elementen Phosphor, Arsen und Antimon waren, die als Quelle toxischer Gase und Ursache von SIDS identifiziert worden sind (Richardson 1990, 1991 a,b,d). Aus jüngeren Berichten geht hervor, dass SIDS in Japan mit einer Inzidenz von 0,4 pro 1.000 Lebengeborene eine größere Bedeutung erhält, ein wesentliches Wachstum in den letzten Jahren, das mit der Aufgabe traditioneller Futons und ihrem Ersatz durch westliche Kindermatratzen zusammenfällt (Watanabe et al 1994).

Cot mattress biodeterioration and toxic gas generation

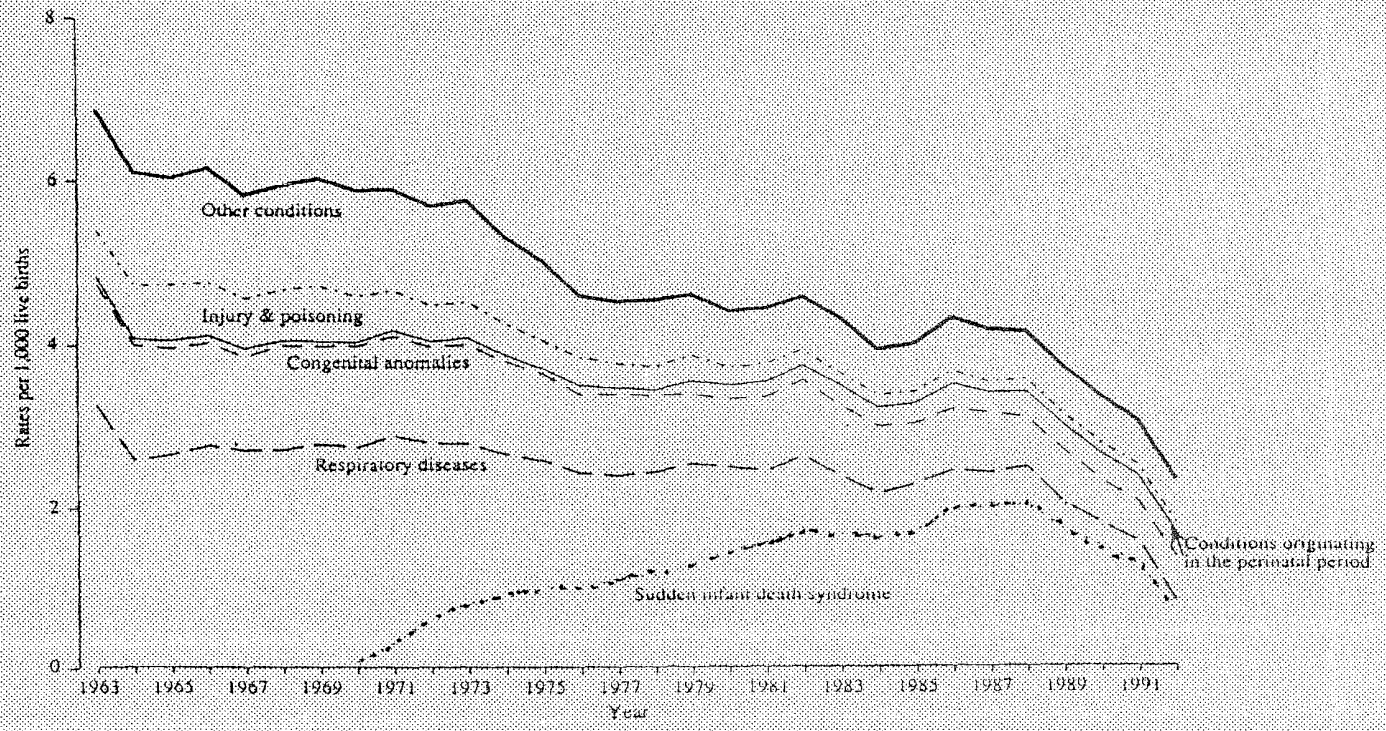

Figure 1. Cumulative postneonatal deaths by selected causes, England and Wales, 1963-1992 (Source: OPCS Monitor DH3 93/2; Crown Copyright 1993)

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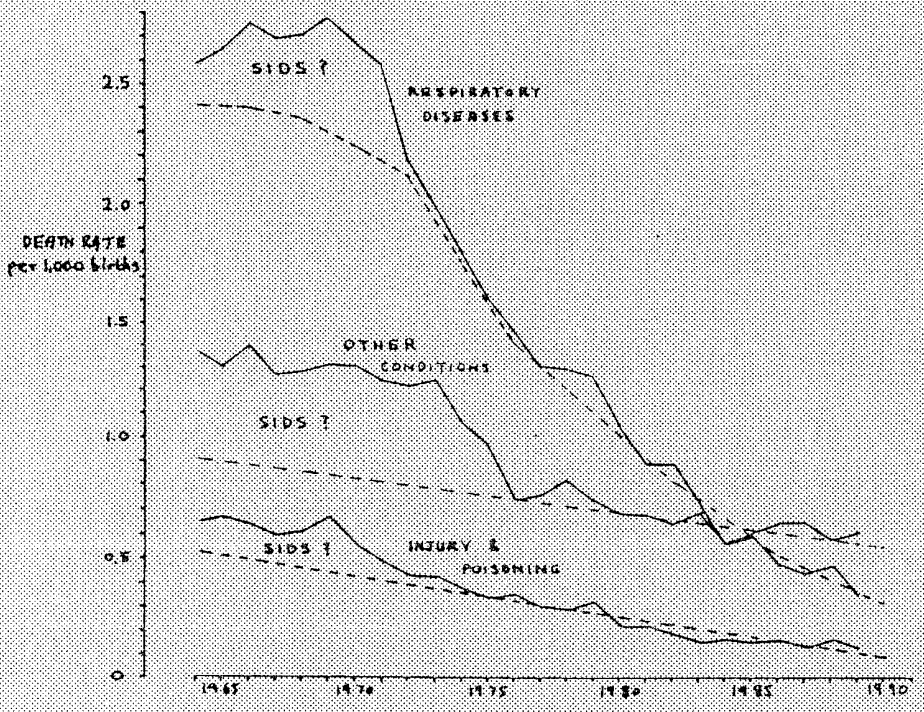

Figure 2. SIDS incorrectly classified under other causes of infant death.

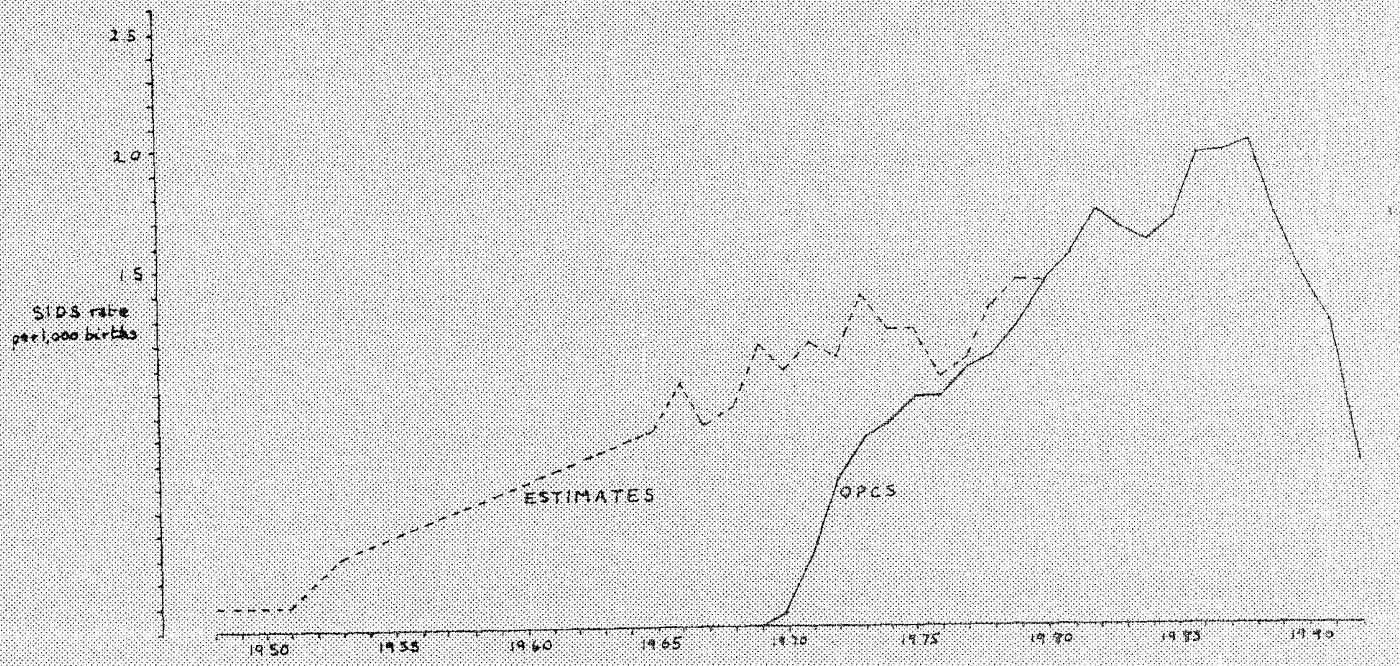

Figure 3. Probable historical development of SIDS, estimated by incorporating corrections deduced from Figure 2.

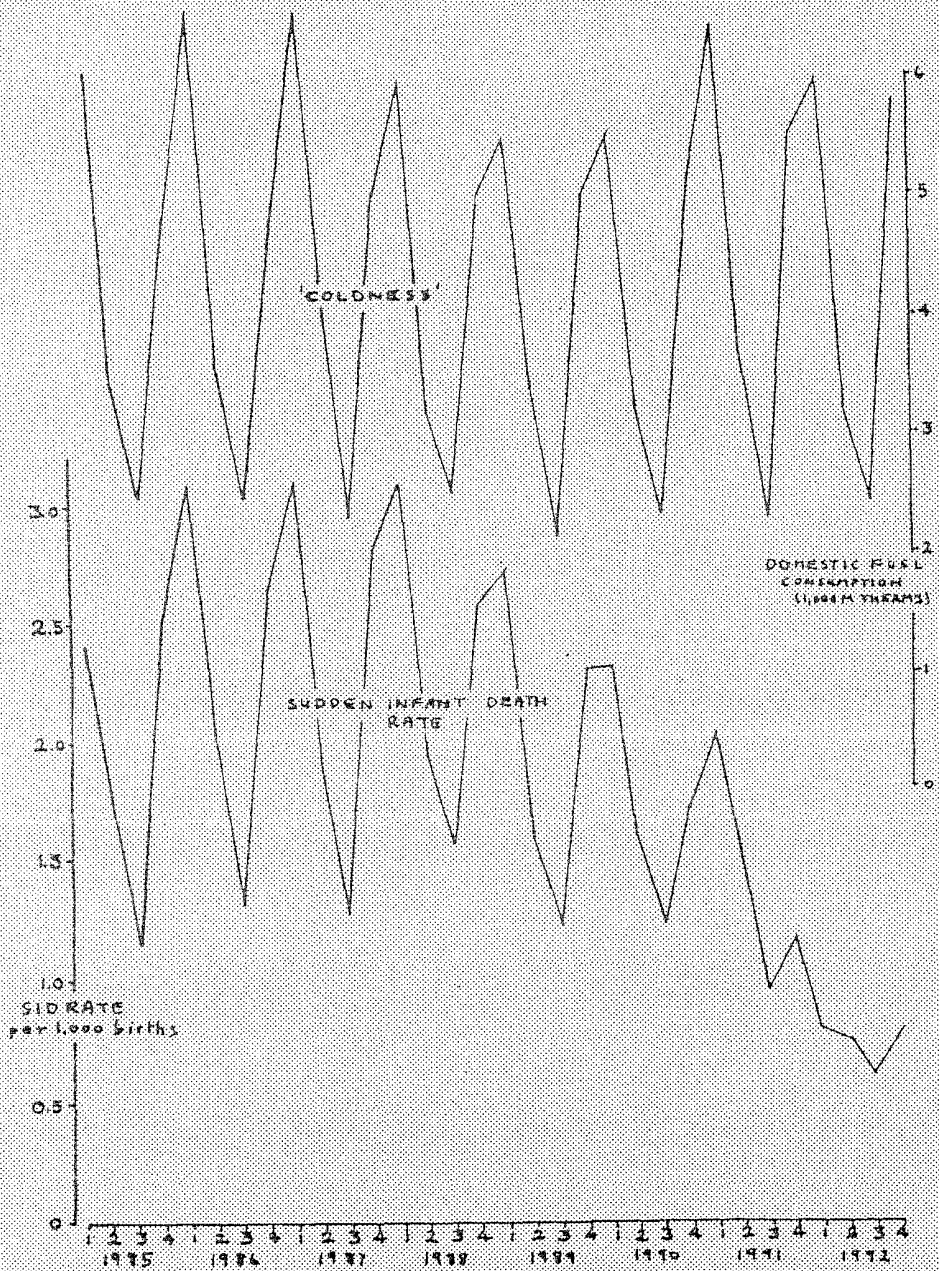

Figure 4. Quarterly SIDS rate for England and Wales, compared with domestic fuel consumption as indication of *coldness*.

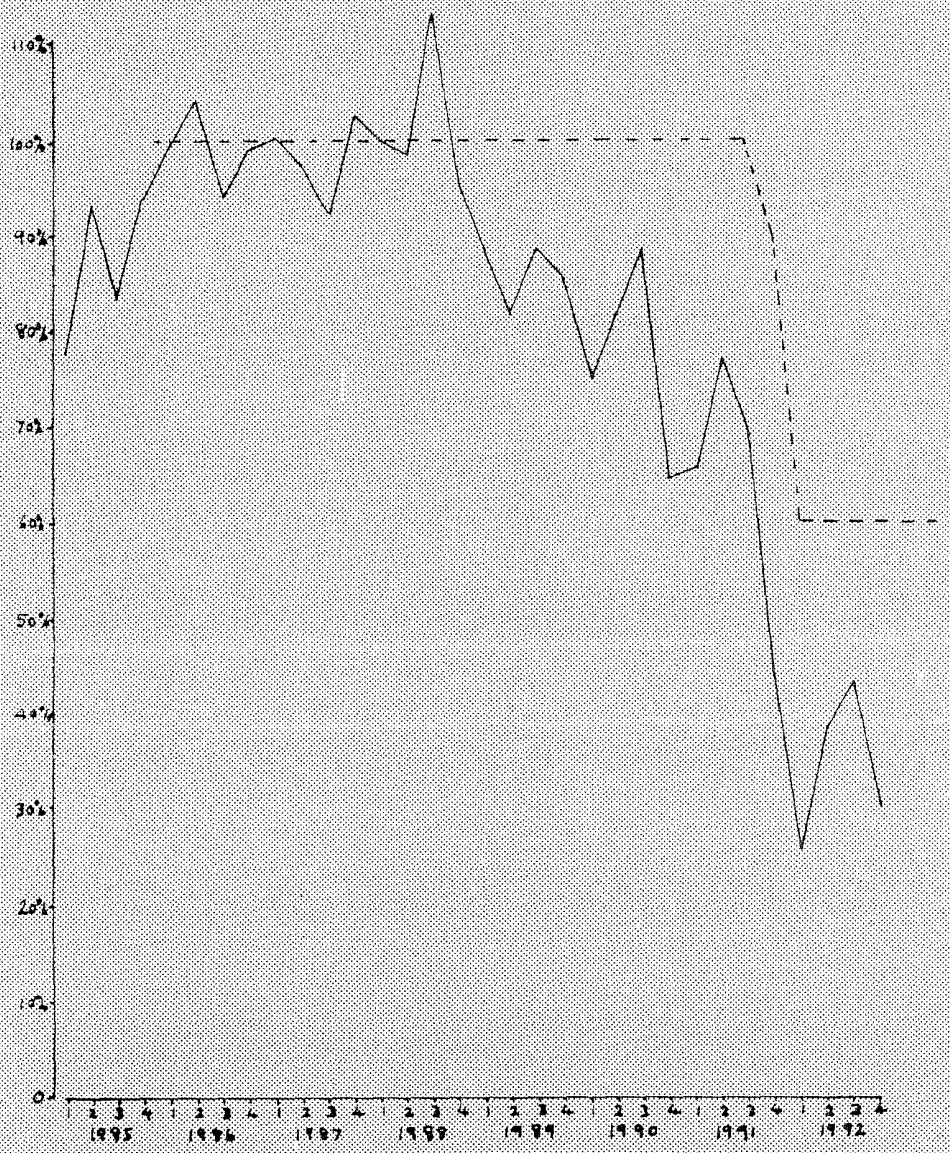

Figure 5. Quarterly SIDS rates, expressed as a percentage of the average rates for the same quarters in 1968-88. Weather fluctuations can be ±12.5%. The pecked line represents the anticipated results of the Department of Health *Back to Sleep* campaign.

Bedding

3.11 Suffocation has always been suspected as a possible cause of SIDS (Meadow 1989). It is certainly true that SIDS victims are often found in the prone position completely covered by bedding and sometimes at the bottoms of their beds, conditions that would be consistent with suffocation but which are equally consistent with hyperthermia and increased exposure to toxic gases generated from mattress materials. Nasal obstruction is increased with some softer mattress materials (Emery Thorton 1968; Emery 1988). However, firmer mattresses covered with impermeable fabric such as PVC may increase the danger of inhalation of vomit by prone infants; this has prompted the introduction in recent years of vented mattresses which comprise foam covered only by a net fabric, but these mattresses do not significantly improve the dispersal of vomit by absorption, and introduce the danger of allergic reactions to spores and mites associated with fungal infections developing on dribble and vomit accummulations in the foam filling materials (Richardson 1991a). Infants on vented mattresses may also be exposed to toxic components in mattress materials by touching, sucking or breathing absorption, or by generation of toxic gases through biodeterioration, toxic hazards that have increased in recent years through more extensive use of fire retardant or combustion modified materials. The risks associated with compounds of phosphorus, arsenic and antimony in mattress materials have already been detailed in the previous chapter (Richardson 1990, 1991 a, b, d, 1994).

3.12 Hyperthermia due to overwrapping in relation to the temperature of the surrounding environment was first suggested as a possible cause of SIDS in 1979 (Stanton 1984; Beal 1988; Stanton et al 1989; Nelson et al 1989). A recent controlled population study has confirmed that SIDS is associated with overwrapping and the prone sleeping position (Fleming et al 1990). Deaths occur particularly in the winter months and in cold climates when parents overwrap their infants in response to low external temperatures, although it has also been observed that many deaths in England and Wales occur early in the morning when the hyperthermia becomes more acute when intermittent central heating increases the accommodation temperature. Overheating is a common problem even with normal infants, about a quarter of them perspiring heavily and half of them throwing off all or some of their bed coverings (Bacon et al 1991). It is probable that the SIDS risk is higher in infants with lower weight and lower activity for their age because they have insufficient strength to dislodge their bed coverings in this way (Hutchinson et at 1979; Masterton et al 1987; Richardson 1990, 1991a). The risk of SIDS is also higher at the weekends when the infant is likely to remain undisturbed in its cot for a longer period (Morris 1986). The increase in SIDS coincides in some countries with improvements in accommodation comfort and higher temperatures in homes but, whilst higher average temperatures have been achieved at different rates in different countries, the SIDS rate has increased relatively steadily between 1950 and 1980 in most western-style countries but has been much lower in eastern countries such as Japan despite similar accommodation temperatures.

3.13 There is extensive evidence that hyperthermia is a contributory factor in SIDS. In 1990 it was suggested that hyperthermia might increase the activity of some natural fungal infections on cot mattresses, and also the rate of generation of the toxic gases that can be released from some mattress materials by micro-organisms (Richardson 1990, 1991a,b,c,d). The toxic gases that are generated in this way are heavier-than-air, and overwrapping will tend to trap these gases within the bedding as well as encouraging hyperthermia and greater gas generation. The higher SIDS rate amongst boys may be due to their higher metabolic rate and their greater susceptibility to hyperthermia when overwrapped.

Sleeping position

3.14 SIDS victims are usually found in their cots in the prone position, and it is now well established that the SIDS risk is greatly increased for infants who sleep in their cots in the prone position (Hassall & Vandenberg 1985; Beal 1988; McGlashan 1988; Davies et al 1989; Engelbert & de Jonge 1990a,b; Fleming et al 1991, 1992). The SIDS rate has been rather lower in the Nordic countries than in the rest of Europe, and in 1976 it was only 0.48 per 1,000 live births, but the supine sleeping position was preferred at that time and the progressive adoption of the prone sleeping position resulted in a significant increase to 0.94 in 1984-86 (Norvenius 1988; Wennegren et al 1987). It was recognised in the Netherlands that the prone position had been adopted to an increasing extent following suggestions at a paediatric conference in 1971, and the SIDS rate increased from about 0.46 per 1,000 births in 1969-71 to about 1.31 by 1978 (de Jonge et al 1989). It was established in the Netherlands that the SIDS risk was about 2.2 times greater in infants that may be prone compared with those that are never prone, and 4.6 times greater in infants that are always prone, whilst in New Zealand the lateral position has been found to increase the risk 2.29 times and the prone position 7.44 times (Mitchell & Engelberts 1991). It was recommended in the Netherlands that parents should avoid the prone sleeping position; the use of the prone position reduced from 60% to less than 30%, and the SIDS rate then decreased by about 40% (Engleberts & de Jonge 1990). Similar recommendations in New Zealand and the State of Victoria in Australia achieved similar reductions (Carpenter & Shaddick 1965; Beal 1988). Recommendations in England in July 1990 that overwrapping and the prone position should be avoided have contributed to a progressive decrease in the SIDS rate, although the decrease was first observed a year earlier following recommendations that every new infant should be provided with a new mattress or old mattresses should be covered with polythene to isolate the infant from the mattress materials; the prone position involves maximum exposure to any toxic heavier-than-air gases generated from the mattress (Engelberts & de Jonge 1990; Fleming at al 1990, 1992; Richardson 1990, 1991a,b,d; Berry 1991). The lower SIDS level in Hong Kong and the very low level in Japan may be due to the preference for sleeping infants in the supine position in these countries (Lee et al 1989; Watanbe et al 1994).

3.15 The prone position may cause hyperthermia, the significant heat loss from the face in the supine position being prevented in the prone position, particularly if the infant is also overwrapped (Nelson et al 1989; Stanton et al 1989; Fleming et al 1992). However, the prone position may also obstruct the large blood vessels in the neck and cause hypoxia (Gilles et al 1979; Levene & McKenzie 1990). It has also been suggested that the prone position may prompt apnoea, either because the infant is more contented in that position and sleeps more deeply, or because the position results in a higher body temperature (Scott 1990; Guntheroth & Spiers 1990). However, the situation is very confusing as there are just as many reports that the head position has no influence on hypoxia, and the prone position improves oxygenation and reduces apnoea (Lawson et al 1987; Wagaman et al 1979; Martin et al 1979; Dhande 1982). It is certainly well established that infants in the prone position are more content as they sleep more readily, they cry less, they move less and they are less likely to suffer from 3 month colic, and the prone position is usually preferred in neonatal units for these reasons (Illingworth 1954; Brackbill et al 1973; Engelberts & de Jonge 1990). It is sometimes suggested that the prone position increases the danger of choking on vomit, and this is the justification of the introduction of vented mattresses in place of mattresses covered by an impermeable fabric, but it is usually considered that the prone position is best and minimises the risk of choking on vomit (Southall et al 1991). The prone position may be associated with the development of nasal

obstruction associated with viral or bacterial respiratory infections but, whilst these may be largely avoided in the supine position, other problems may develop; for example, babies with anatomical abnormalities such as Pierre Robin syndrome (abnormal tongue anchorage and reduced buccal cavity) can only survive in the prone position (Steinschneider 1975; Morris et al 1978; Guilleminault et al 1986; Emery 1988; Nicholl & o'Cathain 1988; Morris 1989; Milner & Ruggins 1989).

3.16 Whilst SIDS victims are usually found in the prone position and avoidance of the prone position can certainly lead to a reduction in the SIDS rate, the prone position is certainly not a primary cause of SIDS but is only a contributory cause. For example, in 1986-88 36% of infants in England were put to sleep in the prone position but only 24% in Scotland, yet the SIDS rate was slightly higher in Scotland during this period at 2.17 per 1,000 births compared with 2.03 for England and Wales (Shapiro et al 1990).

Respiratory and alimentary infections

3.17 It has been suggested that SIDS may be due to unidentified respiratory infections, an hypothesis that was prompted in the United Kingdom by statistical observations which appeared to indicate that the increasing incidence of SIDS was associated with an equivalent decrease in deaths due to respiratory disease, as indicated in figure 1 (Knowelden et al 1984). The progressive reduction in deaths due to respiratory disease actually results from the introduction of improved antibiotics and is seen similarly in other age groups and in most other countries even where SIDS is not reported. Whilst some SIDS deaths were certainly classified as due to unidentified respiratory disease before the separate SIDS classification was introduced and fully recognised, a closer study of this statistical information reveals that most SIDS deaths were classified as 'unexplained' deaths and included in the 'other' classification.

3.18 There is no evidence that overwhelming respiratory disease is a cause of SIDS; indeed, if this was the case it would have been recognised and it would not have been necessary to introduce a separate SIDS classification for cause of death. However, it is generally accepted that there is frequently evidence of respiratory disease which may be a contributory factor in SIDS and which may explain the general malaise that is sometimes reported to effect SIDS victims shortly before death; for example, respiratory viral infections were identified in 38% of SIDS victims compared with only 16% of infants who had died of other non-respiratory causes (Gold et al 1961; Ray et al 1970; Urquhart & Grist 1972; Downham et al 1975; Scott et al 1978; Uren et al 1980; Berry 1992; Essery et al 1994; Murrell et al 1994). It has been suggested that SIDS occurs more frequently during RSV (respiratory syncytial virus) epidemics and whooping cough, yet the SIDS rate is low in Hong Kong despite a high rate of respiratory infection (Williams et al 1984; Davies 1985; Nicoll & Gardner 1988). In a recent study on 37 SIDS victims only 8% were considered to have indications of serious illness prior to death (Cole et al 1991). Whilst an unrecognised respiratory pathogen is a possible cause of SIDS, it must be concluded, as originally suggested in 1954, that acute respiratory inflammation or infection is unlikely to be the primary cause of SIDS, and observed pathological features suggest only mild irritation.

3.1^9 Mild viral or bacterial infections will aggravate hyperthermia caused by overwrapping (Milner & Ruggins 1989). Inflammation in the upper respiratory tract may also increase susceptibility to apnoea caused by closure of the airway on Inspiration; certainly viral infections are often associated with apnoea in otherwise healthy babies (Steinschneider 1975). Bacterial overgrowth of the nasopharynx observed in SIDS victims has also

prompted the suggestion that bacterial infections, perhaps in association with viral infections, may generate toxins which may be a cause of SIDS, a suggestion that can be related to the higher incidence of SIDS in the prone position in which bacterial secretions may accumulate in the upper respiratory passages (Morris et al 1987; Morris 1989). However, whilst these observations may be significant in some cases, it must be recognised that respiratory infections are not identified in the majority of SIDS victims and observed apnoea is just as likely to be caused by bronchial oedema or asthma (Robinson 1994).

3.20 A toxic infection would closely fit the SIDS age distribution with a peak at 3 to 4 months if temperature and immunological status are considered (Morris et al 1987; Murrell et al 1987; Bettelheim et al 1991). Microbial investigations on SIDS victims have detected significantly raised levels of streptococci and certain enterococci, as well as raised levels of Escherichia coli toxin and staphylococcal TSST-1 toxin (Morris et al 1987; Murrell et al 1987; Newbould et al 1989; Bettelheim 1990).

Immune system deficiency

3.21 It has been suggested that SIDS may be associated with immune system deficiencies. High concentrations of Ig A and particularly Ig G and Ig M have been found in the lungs of SIDS victims compared with babies dying from other non-respiratory causes (Forsyth et al 1989). These observations are considered to indicate an abnormal immunological response to a minor infection rather than an overwhelming infection by an unidentified respiratory pathogen, these minor infections perhaps being more significant in relation to hyperthermia (Milner & Ruggins 1989). This abnormal immunological response may be associated with reported faulty formation of haemoglobin and immunoglobins, causing difficulty in transferring from foetal to adult haemoglobin with white cell defects causing difficulty in transferring from a foetal passive to an adult active immune system (Stewart 1989; Matthews & Fox 1989). It is possible that these haemoglobin and immunoglobins defects may be due to poisoning by the toxic gases that are generated by biodeterioration of some mattress materials; certainly arsine poisoning induces a reduced immunological response and phosphine and stibine can be expected to have a similar action, and whilst erythrocyte haemolysis is usually considered to be an esssential diagnostic feature of arsine poisoning in adults, an increase in white cell count may be more significant (Rosenthal et al 1989; Hong et al 1989).

3.22 Eine jüngere Untersuchung referierte Nachweise für eine abnorme durch T Lymphozyten mediierte pulmonale Entzündungsreaktion bei SIDS. Es wird nahe gelegt, dass eine Degranulation der Eosinophilen epitheliale Schäden verursachen kan, wie intrathorakale subseröse petechiale Blutungen und ein pulmonales Ödem wie sie normalerweise bei SIDS gesehen werden, und dass diese Schäden die Ursache einer respiratorischen Obstruktion und Hypoxie sein können, die auch mit SIDS in Zusammenhang steht (Howat et al 1994). Eine alternative Erklärung ist, dass die hohen Werte der Eosinophilen, T und B Lymphozyten und peribronchialen Mastzellen, die berichtet wurden, tatsächlich die Antwort auf Schäden sind, die auf andere Weise verursacht werden, vielleicht durch Vergiftung durch Phosphine, Arsine und Stibine die durch Biodeterioration von Matratzenmaterialien generiert werden und als eine mögliche Ursache von SIDS identifiziert worden sind.

Enzyme dysfunction

3.23 Various enzyme dysfunctions have been suggested as a cause of SIDS. Most of these hypotheses have been concerned with defective metabolism and particularly energy storage and utilization.

3.24 Glucose is an essential constituent in blood, providing the fuel for the body cells. The normal glucose concentration in blood is about 0.1% by weight, lower concentrations initially affecting the function of the nerve cells, particularly in the brain, and prompting muscular twitchings, convulsions and eventually death. Glucose is stored in muscle tissue and in the liver as glycogen, and enzymes are involved in both the storage and release processes. lt has been suggested that SIDS might be due to type 1 glycogen storage disease which is caused by a deficiency of hepatic microsomal glucose-6-phosphatase, obstructing conversion of glycogen to glucose and prompting fatal hypoglycaemia (Cori & Cori 1952; Arion et al 1976; Nilsson et al 1978; Narisawa et al 1978; Arion et al 1980; Lange et al 1980; Burchell & Burchell 1980; Burchell & Burchell 1982; Nordlie et al 1983; Burchell et al 1985; Burchell et al 1987; Waddell & Burchell 1987; Waddell et al 1988; Burchell et al 1988; Countaway et al 1988; Emery et al 1988; Blair & Burchell 1988; Waddell et al 1989; Burchell et al 1989). Glucose-6- phosphatase is not a single enzyme but a complex comprising at least five different polypeptides; a glucose-6-phosphatase enzyme, a regulatory calcium binding protein, and three transport proteins designated T1, T2 and T3 which enable glucose-6-phosphatase, phosphate and pyrophosphate, and glucose respectively to cross the endoplasmic reticulum membrane. Raised hepatic glycogen levels have been detected in more than 25% of SIDS victims, with about 20% diagnosed as type 1a glycogen storage disease involving classic glucose-6-phosphatase deficiency, about 2% as type 1b disease involving T1 deficiency, and about 5% as type 1c involving T2 deficiency (Burchell et al 1989). Severe hypoglycaemia due to type 1 glycogen storage diseases may be a genetic defect, but investigations have suggested that families in which this defect is established do not suffer a significantly higher SIDS rate (Addison et al 1989).

3.25 Some sudden and unexpected infant deaths which might have been attributed to SIDS have been shown to involve genetic defects of fatty acid metabolism (Howat et al 1984; Howat et al 1985; Roe et al 1986; Duran et al 1986; Anon. 1986; Chalmers et al 1987; Harpey et al 1987a; Harpey et al 1987b; Allison et al 1988; Emery et al 1988; Burchell et al 1989). Faulty fatty acid oxidation due to medium-chain acyl coenzyme A dehydrogenase (MCAD) deficiency has been diagnosed in about 5% of SIDS victims, prompted by observations of fatty changes in the liver which are often associated with profound hypoglycaemia. MCAD deficiency is genetic, and the SIDS risk is higher in families in which this condition has been diagnosed (Addison et al 1989).

3.26 Interference with the enzymes involved in muscle contraction and relaxation has also been suggested as a possible cause of SIDS (Denborough 1989). Nerve impulses prompt the formation of IP3 at the muscle which releases calcium from the muscle cell, causing the protein in the muscle to contract. The increasing calcium concentration outside the muscle cell then stimulates a phosphatase which breaks down the IP3 to IP2 which is inert, allowing the muscle protein to relax. Deficiency of the IP3 phosphatase results in protracted muscle contraction which is sometimes a cause of death in anaesthesia, but this condition is also associated with hyperpyrexia or hyperthermia, and death may be due to heat stroke, suggesting a link with SIDS in which hyperthermia is often observed.

3.27 Phosphoenolpyruvate carboxykinase deficiency in the liver has also been suggested as a cause of SIDS, but this hypothesis has not attracted any recent attention (Sturmer Susa 1980).

3.28 It has been suggested that SIDS might be caused by an anticholinesterase poison (Richardson 1991a, b, d, 1994). Acetylcholine is generated at nerve endings, stimulating the next nerve and providing continuity of impulse across a nerve synapse, although this

system can only operate if cholinesterase is present which steadily reduces the acetylcholine concentration so that the next impulse and release of acetylcholine can be detected. Acetylcholine is also released by the vagus nerve into the blood stream, regulating cardiac activity in infants by inhibiting smooth muscle contraction. Cholinesterase in the blood normally ensures that acetylcholine is destroyed before the blood next enters the right atrium of the heart and receives more acetylcholine from the vagus nerve, but if the cholinesterase in the blood is depressed, acetylcholine will progressively accumulate, inhibiting cardiac contractions until death eventually occurs. Phosphine, arsine, stibine and associated alkyl compounds which are generated through biodeterioration of cot mattress materials containing fire retardents and preservatives are known to interfere with the central nervous system in adults through anticholinesterase action, but in infants this poisoning is more likely to result in cardiac failure, which would be completely consistent with SIDS with its absence of significant pathological features.

3.29 Enzymes are proteins, usually containing heavy metals, which can be inactivated by compounds such as cyanides which will complex with the heavy metals. Other poisons may be absorbed onto reactive sites on the molecule, destroying the enzymatic action; phosphine, arsine and stibine dissolve in blood to form phosphonium, arsonium and stibonium cations which can behave in this way but which, if present in sufficient concentration, may also condense onto blood glucose units, preventing glucose metabolism and prompting cell death. However it is more likely that the anticholinesterase action of phosphine, arsine anad stibine involves the substitution of phosphorus, arsenic or antimony in place of nitrogen in the cholinesterase protein.

Hyperthermia and hypothermia

3.30 Hyperthermia or hyperpyrexia is often observed in SIDS victims, and is usually attributed to overwrapping in relation to the temperature of the surrounding environment at the time of death. Hyperthermia does not seem to be a cause of death as the characteristic tissue damage associated with heatstroke is not normally observed, although there are reports that where twins are sleeping in the same room and one is a SIDS victim, the other often suffers haemorrhagic shock encephalopathy syndrome which has clinical and pathological features similar to heatstroke (Wadlington et al 1976; Bacon et al 1979; Trounce et al 1991; Bacon 1991). HSES (Haemorrhagic shock encephalopathy syndrome) may therefore result from hyperthermia and SIDS may be caused by hyperthermia in more sensitive individuals who die before development of the tissue damage which is characteristic of heat stroke, although it is more likely in twins that the SIDS victim was on a previously used mattress generating toxic gases and the HSES victim was on a new mattress free from toxic gas generation.

3.31 Hyperthermia prompts hyperventilation and a decreasing carbon dioxide tension in the blood which may in turn inhibit ventilation and prompt apnoea. The respiratory centre in the medulla is not well developed in young infants who depend instead on chemoreceptors in the carotid sinus which react particularly to carbon dioxide tension, but hyperthermia may cause dysfunction of this respiratory chemoreceptor (Gozal et al 1988; Bacon 1991.)

3.32 Whilst hyperthermia is certainly associated with SIDS and usually caused by overwrapping, aggravated by mild infections and other complications such as genetic phosphatase deficiency in muscle tissue, there is no evidence that hyperthermia is itself a cause of SIDS, but it is probably an important contributory factor, particularly in relation to the generation of toxic gases from mattress materials (see Appendix 2). Normal healthy infants affected by hyperthermia dislodge and remove bed coverings but weaker infants may not be able to react in this way and this may explain why the SIDS risk is greater for infants which are

underweight for their age (Bacon et al 1991). Boys may be more sensitive to hyperthermia because of their higher metabolic rate and this may explain why the SIDS risk in boys is about 50% greater than in girls.

3.33 Whilst hyperthermia is reported in almost all SIDS victims, there have been some reports of hypothermia (Dunne Mathews 1988). Hypothermia may be due to inadequate wrapping in relation to the environmental temperature, but temperature control is very efficient in normal healthy infants and hypothermia therefore is likely to be an indication of faulty metabolism, probably inefficient glycogen or fatty acid utilisation due to enzyme deficiency, perhaps a genetic defect.

Apnoea

3.34 The SIDS risk is higher in infants which are susceptible to prolonged apnoea, and cyanosis is often present in SIDS which indicates anoxaemia caused by cardiac or respiratory failure (Steinschneider 1975; Kelly et al 1986; Morris et al 1987; Kahn et al 1988; Schechtman et al 1991). It has been suggested that the risk of SIDS can be predicted by investigations of apnoea and disorders of cardiac rhythm but, in a survey of 9,000 infants, the 29 SIDS victims were not recorded as suffering previous apnoea or other respiratory abnormalities (Southall 1983; Southall et al 1985). It has not been established whether susceptibility to apnoea is a contributory factor in SIDS or whether the apnoea is prompted by a condition which is also a cause of SIDS, but there are many reports now of abnormalities in cardiac and respiratory regulation which seem common to both SIDS and apnoea so that at least some cases of apnoea are likely to be near-miss SIDS incidents (Schechtman et al 1991; Hunt 1992; Matturri et al 1992; Pincus et al 1993; Keens & Ward 1993). If apnoea follows cardiac failure, monitors indicate a progressive decrease in the heart rate which, if continued, would be completely consistent with the symptoms of SIDS, particularly if the primary cause of SIDS is anticholinesterase poisoning, but obstructive apnoea, whatever the cause, is characterised by an increasing heart rate prompted by respiratory distress (Hoppenbrouwers et al 1993). Respiratory distress and an increased heart rate may therefore be an indication of respiratory obstruction through bronchial oedema or asthma (Robinson 1994). Apnoea may be due to obstruction of the upper respiratory tract such as closure of the oropharynx and hypopharynx in inspiration to which an infant may be more susceptible in the prone position (Kahn et al 1988; Southall et al 1989). The risk of SIDS is higher in infants subject to prolonged apnoea, even if the attacks are not considered to be severe (Kelly et al 1986; Kahn et al 1988). Obstructive apnoea may be associated with respiratory infection and inflammation in the upper airway (Steinschneider 1975).

3.35 In adults the respiratory centre in the medulla is responsible for respiratory control, but this system is not well developed in young infants who depend instead on a respiratory centre in the carotid sinus. Overheating due to overwrapping may induce hyperventilation and a reduction in the carbon dioxide tension in the blood which may in turn inhibit ventilation and prompt apnoea. Poisoning by gases which will form bases in the blood will absorb carbon dioxide and similarly prompt apnoea.

3.36 Expiratory apnoea may cause arterial hypoxaemia and, in extreme cases, may induce cyanosis and hyperthermia, symptoms which are often associated with SIDS (Southall et al 1985; Dunne Mathews 1988).

Hypoxia

3.37 It has been observed that hypoxanthine concentrations in vitreous humour are very high in SIDS victims compared with infants dying from other nonrespiratory causes (Rognum

et al 1988; Rognum & Sangstad 1991). Hypoxanthine is formed from adenosine monophosphate by a catabolic process which is accelerated by hypoxia, so that these observations suggest hypoxic conditions at death. There are many other indications of hypoxia in SIDS such as extramedullary haemopoiesis in liver (Berry 1993). Hypoxia can be caused by various metabolic defects, by respiratory failure such as apnoea, or by cardiac failure, perhaps caused by poisoning by toxic gases generated by mattress deterioration (Southall 1983; Southall et al 1985; Gozal et al 1988; Southall Samuels 1989; Richardson 1990, 1991 a, b; Bacon 1991). Oxygen monitors can detect the onset of hypoxaemia in infants but will not necessarily avoid SIDS; hypoxaemia may not be a cause of SIDS but may be simply an associated symptom (Poets et al 1991).

Allergic reactions

3.38 Exposure to spores and mites from fungal infections on bedding may cause sensitization and eventually fatal asthma attacks (Gravesen 1979; Homberg & Kallings 1980; Sundin 1983; Anon. 1984; Barr et al 1985; Holmberg 1985; Croft et al 1986; Milberg 1987; Richardson 1991a). Many of the fungal infections that develop on mattress materials are known to induce asthma in this way, but there is no evidence that this is a major cause of SIDS, although it would be consistent with observed hypoxia.

3.39 The incidence of asthma in older children in the British Isles has increased over the last eighteen years. This increase may be associated with increased exposure to heavier infections in the cot environment (Richardson 1991d, 1994). Mattresses covered with easily cleaned impermeable PVC fabric are being progressively replaced by vented mattresses in which the foam filling is covered only by net, encouraging the development of heavy bacterial and particularly fungal infections where the exposed foam is affected by perspiration, dribble and vomit. The fungal infections are species producing spores commonly associated with asthma; fungal infections also support mite colonies which are also associated with asthma.

Other factors

3.40 Many possible causes of SIDS have been suggested. Prior to 1954 it was always considered that the most likely cause was deliberate or accidental suffocation, and it has been suggested as recently as 1989 that 2 to 10% of SIDS victims could have been smothered deliberately (Meadows 1989). Detailed studies of 988 infant deaths in 1976--79 identified only about 1% as infanticide and 1.5% as suspicious (Knowelden et al 1984). The SIDS rate at that time was about 2.0 per 1,000 live births and infanticide may therefore have accounted for up to 0.05 deaths per 1,000, about half of the sudden unexplained infant death rate prior to 1950 which was only about 0.1 per 1,000, a comparison that also explains the serious concern at the current SIDS rates, typically 2 to 4 per 1,000 in affected countries.

3.41 It has been frequently suggested that SIDS is caused by exposure to electromagnetic radiation. Strong electro-magnetic fields can affect persons, and some individuals are particularly sensitive to certain frequencies, but there is no evidence of consistency between SIDS and possible exposure to various forms of electro-magnetic radiation.

3.42 Congenital defects such as adrenal hypoplasia and islet hyperplasia have been suggested as possible causes of SIDS (Polak & Wigglesworth 1976; Russell et al 1977). However, whilst these conditions may be a primary or contributory cause in some individual cases,

there is no evidence that they are generally associated with SIDS. Congenital enzyme deficiencies related to metabolism are much more likely causes of SIDS, and may be related to the observed islet hyperplasia, but they have still been observed in only a small proportion of SIDS victims.

3.43 Lethal toxic infections would be consistent with SIDS in terms of the peak age distribution of about 3 to 4 months when temperature and immunological status are considered (Morris et al 1987; Murrell et al 1987; Bettelheim et al 1991). Toxic respiratory and alimentary infections have been considered earlier.

3.44 Gaseous poisoning has also been proposed as a possible cause of SIDS. The association with overwrapping suggests that limited ventilation might result in an accumulation of carbon dioxide and increasing carbon dioxide tension in the blood which would prompt hyperventilation, but the respiratory chemoreceptor in the carotid Sinus in infants may be blocked in hyperthermia, preventing hyperventilation and allowing carbon dioxide to accumulate to dangerous concentrations. Excessive accumulations of carbon dioxide may result eventually in formation of carbon monoxide and methaemoglobin in the erythrocytes, obstructing oxygen transport in the blood, but carbon monoxide poisoning is unlikely as the gas is lighter-than-air and readily disperses from bedding, and the well established symptoms of carbon monoxide poisoning have never been reported in SIDS. Rebreathing on a soft mattress such as sheepskin has been considered as a source of carbon dioxide and a cause of SIDS (Elfast 1994).

3.45 Ammonia, generated by bacterial degradation of urine, has also been suggested as a possible cause of SIDS but it is lighter-than-air and readily disperses from bedding; this is why it is noticed by parents. However, ammonia is the trihydride of nitrogen, an element in Group V/Vb of the chemical periodic table, and similar biodegradation of compounds containing the other elements in this group phosphorus, arsenic and antimony can generate much more toxic heavier-than-air gases which will accumulate on cot mattresses, particularly when an infant is overwrapped, presenting a particular hazard to infants sleeping in the prone or face down position.

Im vorausgehenden Teil dieses Berichts wurde erklärt, dass die generierten Gase Phsophin, Arsin und Stibin Nervengifte mit einer Anticholinesterase-Wirkung sind und bei Babies höchstwahrscheinlich fatal mit der kardialen und respiratorischen Regulation interferieren (Hunt 1992, Matturri et al 1992; Pincus et al 1993). Ein Herzversagen durch zunehmende Akkumulation von Acethylcholin wurde als Ursache von SIDS schon vorgeschlagen und einer Dysfunktion des Vagus zugeschrieben, obwohl die Symptome mit einer Anticholinesterase-Vergiftung identisch sind (Farber et al 1983; Greenwald 1984). Abnormitäten des Nervensystems wurden berichtet die von einer Anticholinesterase-Vergiftung kommen aber alternativ auch die Empfindlichkeit gegenüber dieser Vergiftungsform erhöhen können (Kinney et al 1991; Speights & Bauserman 1991; Becker et als 1993; Filano & Kinny 1994; Kopp et al 1994). Verzögerte oder abnorme Entwicklung des Nervensystems, insbesondere verzögerte Myelinisierung, scheint in Zusammenhang mit Babies vorzukommen, die nicht oder nur für eine kurze Zeit gestillt worden sind; Kuhmilch und andere Säuglingsnahrungsformeln sind in Bezug auf die Fettsäuren, die bei der Myelinisierung eine Rolle spielen, defizient (Kenny et al 1991; Speights & Bauserman 1991; Ford et al 1993).

4. Schlussolgerungen und Empfehlungen

4.4 Konservierungs- und Flammschutzmittel in Matratzen-Füllungen und -Hüllen die Phosphor, Arsen und Antimon enthalten wurden alas Quellen der extrem giftigen Phosphine, Arsine und Stibine identfiziert, die durch natürliche fungale Verrottung als Gase freigesetzt werden. In England und Wales sind Veränderungen der Matratzenherstellung und -Zusammensetzung auf die steigenden SIDS-Ziffern zwischen 1951 and 1988 bezogen werden, und weithin publizierte Empfehlungen im Juni 1989 dass alle neuen Babies eine neue Matratze erhalten sollten (alte Matratzen sollten mit Polyethylen bedeckt werden, um die Babies von den Matratzenmaterialien zu trennen) führten zu einem Anwachsen des Verkaufs neuer Matratzen, auf das ein progressiver Rückgang der SIDS-Inzidenz folgte. Auf den Beginn der *Schlaf auf dem Rücken*-Kampagne des Department of Health im November 1991 folgte für eine kurze Zeit ein noch rascherer Rückgang, aber der stetige Rückgang setzte sich seitdem augenscheinlich als Resultat der fortschreitenden Reduktion des Phosphor-, Arsen- und Antimongehalts der Matratzenmaterialien fort. In England und Wales betrug die Inzidenz der plötzlichen Todesfälle bei Kindern (das sind hauptsächlich SIDS-fälle) von 2.30 pro 1.000 Lebendgeburten 1988 verminderte sich aber in den Jahren 1989, 1990, 1991, and 1992 auf 1.94, 1.70, 1.44 bzw. 0.77, und wahrscheinlich etwa 0.4 im Jahr 1993.

4.2 Obwohl die Verwendung von Phosphor-, Arsen- und Antimonverbindungen in Matratzen Materialien als Resultat der zunehmenden Intensität der Publizität in den Medien in den letzten 6 Jahren jetzt praktisch beended wurde, haben die meisten Babies in den letzten Jahren auf Matratzen geschlafen, die diese Materialien enthalten, aber die meisten Babies sind nicht gestorben. Ob ein Baby durch diese toxischen Gase nicht beeinträchtigt wird, oder Kopfschmerzen erleidet, Krankheit oder Tod hängt von mehreren zusätzlichen Faktoren ab, die identifiziert worden sind. Deren wichtigster ist die das Schlafen des Kindes auf dem Bauch, das zur höchsten Belastung mit diesen Gasen führt, die schwerer sind als Luft und eine übermäßige Bedeckung, die die Gase um das Kind einfängt und zu einer überwärmung führt, die die Geschwindigkeit der Gasgeneration erhöht.

4.3 Die Opfer des plötzlichen Kindstodes sterben normalerweise auaf Matratzen die vorher von anderen Babies benutzt worden sind und in welchen sich die fungalen Infektionen gut etabliert haben; die SIDS-Ziffern sind am niedrigsten für Erstgeborene und sozial besser gestellte Gruppen, da bei diesen Gruppen der Gebrauch neuer Matratzen am wahrscheinlichsten ist. Die Reaktivierung der auf einer schon benutzten Matratze etablierten fungalen Infektion durch Perspiration und Wärme benötigt gewöhnlich mehrere Wochen , und das ist der Grund dafür, das der plötzliche Kindstod bei Babies unter dem Alter von einem Monat selten ist; Todesfälle in dieser sehr jungen Altersgruppe stehen immer in Zusammenhang mit dem Schlafen auf einer Matratze, die zu dieser Zeit von im Gebrauch eines älteren Kindes ist, in der die fungale Entwicklung und Generation giftiger Gase bereits aktiviert worden ist. Kopfschmerzen sind das erste Vergiftungssymptom, die bei älteren Kindern zur Irritabilität führen, weshalb sie dann ihre Bettdecke lüften, weshalb Todesfälle bei Kindern über einem Alter von 5 Monaten selten sind, aber bei Kindern, die weniger aktiv und weniger fähig sind, ihre Bettdecke zu lüften weil sie ein geringes Gewicht für ihr Alter haben oder ihre Aktivität auas einem anderen Grund unterdrückt ist reicht das SIDS-Risiko bis zu einem Alter von etwa 14 Monaten. Leichte und sonst nicht bedetsame bakerielle oder virale Infektionen können das SIDS-Risiko auf zwei verschiedene Arten erhöhen: die Hyperthermie wird verschlimmert und die Anwendung von Analgetika unterdrückt die Kopfschmerzen die das Baby dazu anregen die Bettdecke zu lüften und die giftigen Gase zu verdünnen.

4.4 Organophosphor-Pestizide und chemische Kampfstoffe sind gut bekannte Nervengifte. Nerven sind durch Synapsen miteinander verbunden in denen das von einer Nervenendung generiertte Acetylcholin den nächsten Nerv stimuliert um den Impuls weiter zu geben, aber das Acethylcholin muss andauernd durch das Enzym Cholinesterase zerstört werden, damit der nachfolgende Impuls mit seinem Acetylcholinreiz wahrgenommen werden kann. Organophosphorverbindungen interferieren mit dieser Cholinesterase so dass sich das Acethylcholin progressiv ansammelt und die Nervenfunktion und besonders die Hirnfunktion blockiert. Phosphin und die verwandten Alkylverbindungen die durch Biodeterioration aus Matratzenmaterialien generiert werden, die Phosphat-Weichmacher und -Flammschutzmittel enthalten sind die einfachsten Organophosphorverbindungen, und es ist deshalb nicht verwunderlich dass von diesen Verbindungen und den mit ihnen verwandten Verbindungen aus Arsen und Antimon eine Anticholinesterase-Aktivität berichtet worden ist. Bei Babies hat Acethylcholin eine besonders wichtige Funktion, da es durch den Nervus vagus als ein Mittel zur Regelung der Herzfrequenz ins Blut abgegeben wird, die Cholinesterase normalerweise das Acethylcholin bevor das Blut wieder zum Herzen zurückkehrt zerstört, wenn die Cholinesterase im Blut aber durch Vergiftung mit Phosphin, Arsin, Stibin oder verwandten Alkylverbindungen zerstört wird, sammelt sich das Acethylcholin im Blut progressiv an und führt letzdendlich zu einem Herzversagen, das mit allen bei SIDS beobachteten Erscheinungen übereinstimmt. Ein Herzversagen verhindert die Sättigung des Blutes mit Sauerstoff und würde die Zyanose erklären,die oft berichtet wird und die Hypoxie oder geringe Sauerstoffsättigung in den Zellen, die offensichtlich immer mit SIDS zusammenhängt.

4.5 Empfehlungen zu Veränderungen der Baby-Versorgungspraktiken, die die Belastung mir Gasen oder deren Generation vermindern, vor allem die Vermeidung des Schlafens auf dem Bauch und übermäßiges Zudecken haben in allen Ländern, in denen diese Interventionen versuch wurden, zu einem Rückgang der SID-Inzidenz von etwa 40% geführt, was dafür spricht, dass diese Empfehlungen nur zusätzliche Ursachen ansprechen. Im Gegensatz dazu betrug der Rückgang von SID in England und Wales zwischen 1988 und 1993 etwa 83% und die Inzidenz nimmt weiterhin ab. England und Wales unterscheiden sich von allen anderen Ländern, weil dort außerdem empfohlen wurde, die Matratzen betreffende Vorsichtsmaßnahmen zu ergreifen, diese größeren Rückgänge sprechen dafür, dass diese Vorsichtsmaßnahmen entweder sehr bedeutsame zusätzliche Ursachen ansprechen, die noch nicht identifiziert worden sind, oder die primäre Ursache.

Empfehlungen

1. Es wird empfohlen Phosphor-, Arsen- und Antimonverbindungen in Matratzenmaterialien sofort zu verbieten. Wenn Flammschutz- oder Konservierungsmittel erforderlich sind, können andere Systeme verwendet werden. Für Matratzenhüllen sind Flammschutzmittel nicht erforderlich, obwohl Füllungen flammresistent sein oder mit einem resistenten Gewebe unterhalb der allgemeinen Hülle bedeckt sein müssen; manches Matratzenmaterial ist von Nautr aus flammresistent. Im technischen Sinn sollten der Gehalt an Phosphor weniger als 0,05%, und der Gehalt an Arsen und Antimon weniger als 0,01% betragen. Einige Polyester-Fasern hat einen Antimongehalt von bis zu 0,02% durch Rückstände eines Produktionskatalysators, eine Höhe die für kurze Zeit toleriert werden, binnen eines Jahres aber eliminiert werden sollte; geeignete Alternative sind vorhanden.

2. Ein Verbot von Phosphor-, Arsen- und Antimonverbindungen in Kindermatratzen wird den plötzlichen Kindstod nur auf längere Sicht eliminieren. Daher ist eine kurzfristige Vorsorge notwendig; die geeignetste ist die feste Umhüllung jeder für mehr als zwei Monate gebrauchten Matratze mit einer Polyethylen-Folie deren Enden unterhalb der Matratze mit Verpackungsklebeband befestigt sind. Polyethylen ist ungiftig und enthält keine Zusätze, und diese Umhüllung isoliert das Baby von den Matratzenmaterielien, was die Belastung mit giftigen Matratzengasen vermindert und auch die Gas-Generation reduziert, indem die Matratze trocken gehalten wird. Eine Matratze die fest mit Polyethylen umwickelt ist ist in iher Textur und ihren Eigenschaften mit einer konventionellen PVC-gedeckten Matratze identisch.

3. Es wird empfohlen die Begrenzung von Phosphor, ARsen und Antimon auf alle Matratzen auszudehnen und vielleicht auch auf alle Einrichtungen das sie auch ein unnötiges Risiko für sitzende Erwachsene darstellen; obwohl unwahrscheinlich ist , dass irgendwelche generierten Gase zu Todesfällen führen werden, können sie Kopfschmerzen hervorrufen und manchmal noch ernstere Wirkungen im Zentralnervensystem. Gosio's Krankheit bei der vor etwa hundert Jahren Arsin aus feuchten Tapeten generiert wurde hat Todesfälle bei Kindern und weitverbreitete Krankheit bei Erwachsenen hervorgerufen.

4. Es wird empfohlen, von Kindermatratzen mit nicht, oder nur mit Netz oder offen gewebtem Stoff bedeckten Schaumstoffen abzuraten. Matratzen dieser Art werden mit Speichel und Erbrechen kontaminiert und können nicht gereinigt werden. Unvermeidlich etablieren sich vielerlei Mikroorganismen, die Sporen bilden und Milben unterstützen die in Zusammenhang mit Asthma stehen; diese Art von atmungsaktiven oder 'Sicherheits'-Matratzen wurde vor etwa 18 Jahren eingeführt und man fand seitdem ein progressives anwachsen von Asthma bei Kindern.

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